Flame Retardant Alternatives

(An assessment of potential health and environmental impacts of RDP and BAPP, two phosphate-based alternatives to Deca-BDE for use in electronics.)

Conducted by Syracuse Research Corporation
for the
Washington State Departments of Ecology and Health,
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1.0 INTRODUCTION

The Washington State Department of Ecology is collecting and compiling data to characterize the hazards of and potential exposures to Phosphoric trichloride, reaction products with bisphenol A and phenol [CAS # 181028-79-5] and Phosphoric acid, 1,3-phenylene tetraphenyl ester [CAS # 57583-54-7], which are potential alternative chemicals that may be used to replace the flame retardant decabromodiphenyl ether (Deca-BDE) in electronic enclosures. Based on the potential for risk to the general public, and children in particular, from the possible widespread use of these alternatives in consumer products, it is important to identify any potential hazard concerns for these flame retardant alternatives in order to mitigate risk whenever possible.

Syracuse Research Corporation is providing the Washington State Department of Ecology with toxicological and environmental fate modeling services to evaluate the hazards associated with the potential use of these alternate flame retardants. In support of this effort, Syracuse Research Corporation has reviewed the toxicity and environmental fate and transport data which have already been compiled by the Washington State Department of Health for the Chemical Action Plan's alternatives assessment. Additional data gathering and literature search efforts have been conducted and the EPA's Office of Pollution Prevention and Toxics' (OPPT) Structure Activity Relationship (SAR) predictive methodologies were used to fill in the identified data gaps.

While reviewing the literature, it became apparent that the name and CAS number for phosphoric acid, 1,3-phenylene tetraphenyl ester [CAS # 57583-54-7] is frequently used interchangeably with the name and CAS number for phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester [CAS # 125997-21-9]. It is believed that the material used by industry for these applications is actually the polymeric material [CAS # 125997-21-9], and not the pure material [CAS # 57583-54-7], which is its major component. For this reason, the hazard assessments were performed on all of the major components of Phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester [CAS # 125997-21-9], instead of focusing solely on phosphoric acid, 1,3-phenylene tetraphenyl ester [CAS # 57583-54-7].

The substances phosphoric trichloride, reaction products with bisphenol A and phenol [CAS # 181028-79-5] and phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester [CAS # 125997-21-9] are both mixtures which contain a number of different chemical components. Since these substances are mixtures, their physical/chemical, environmental and toxicological properties can change depending on the varying amounts of the different components in the mixture. In order to develop consistent and accurate hazard assessments, the assessments must be performed on pure materials rather than on mixtures. Therefore, hazard assessments were performed on the three primary components of each mixture.

The three major components of phosphoric trichloride, reaction products with bisphenol A and phenol [CAS # 181028-79-5] are:

- Phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester [CAS # 5945-33-5]
- Phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-methylethyl]phenyl] phenyl ester [CAS # 83029-72-5]
- Triphenyl phosphate [CAS # 115-86-6].

The three major components of Phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester [CAS # 125997-21-9] are:

- Phosphoric acid, 1,3-phenylene tetraphenyl ester [CAS # 57583-54-7]
- Phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester [CAS # 98165-92-5]
- Triphenyl phosphate [CAS # 115-86-6].

Other higher molecular weight oligomers are also expected to be present in each mixture, but are probably present at less than 2%. Due to the low amount of these higher oligomers and their high molecular weight, they are expected to be of low environmental and toxicological concern.

The assessments presented in this document use the endpoints, models and methodologies of the EPA's Office of Pollution Prevention and Toxics (OPPT), as demonstrated in the EPA's 2005 report, Environmentally Preferable Options for Furniture Fire Safety. This report is available online at: http://www.epa.gov/opptintr/dfe/pubs/flameret/ffr-alt.htm.

The hazard assessments are presented in three different sections. The first section will contain a table with a quantitative summary of the toxicological and exposure characteristics of the chemicals in each mixture. Each toxicological endpoint is assigned a rating of L, M, or H to indicate whether the chemical has a low (L), medium (M) or high (H) hazard concern. Each exposure endpoint is assigned a rating of Y (yes) or N (no) to indicate if that exposure route is expected to occur for each chemical. The second section contains summaries of the physical/chemical, environmental fate and toxicity data that were used to develop the hazard concerns and exposure conclusions that are presented in the quantitative summary table in the first section. The third section contains detailed reviews of the available information on each endpoint for each of the chemicals assessed.

2.0 Summary of Flame-Retardant Chemical Alternatives

Table 2-1 presents a qualitative summary of toxicological and exposure characteristics of the chemicals in each formulation considered in the alternatives analysis. The table qualitatively summarizes toxicological endpoints and exposure routes for each chemical, including seven human health effects, two ecotoxicity effects and two environmental endpoints and six routes of occupational, general population and aquatic exposure. Each of these endpoints is explained in Table 2-2.

Table 2-1 Screening Level Toxicology and Exposure Summary

L = Low hazard concern
M = Moderate hazard concern
H = High hazard concern
L, M, or ***H*** = Endpoint assigned using estimated values and professional judgment (Structure Activity Relationships)

N = No
Y = Yes

Chemical	CASRN	Human Health Effects							Ecotoxicity		Environmental		Potential Routes of Exposure						
													Worker			General Population			
		Cancer Hazard	Skin Sensitizer	Reproductive	Developmental	Neurological	Systemic	Genotoxicity	Acute	Chronic	Persistence	Bioaccumulation	Inhalation	Dermal	Ingestion	Inhalation	Dermal	Ingestion	Aquatic
Phosphoric trichloride, reaction products with bisphenol A and phenol	181028-79-5	***L***	**L**	***L***	**L**	***L***	**M**	**L**	***H***	***M***	**H**	***L***	N	Y	Y	N	Y	Y	Y
Phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester	5945-33-5	***L***	***L***	***L***	***L***	***L***	***M***	***L***	***L***	***L***	***H***	***L***	Y	Y	Y	N	Y	N	N
Phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester	83029-72-5	***L***	***L***	***L***	***L***	***L***	***M***	***L***	***L***	***L***	***H***	***L***	Y	Y	Y	N	Y	N	N
Triphenyl Phosphate	115-86-6	***L***	**L**	**L**	**L**	**L**	**M**	**L**	**H**	***H***	**L**	**L**	Y	Y	Y	Y	Y	Y	Y
Phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester	125997-21-9	***L***	**L**	**L**	**L**	***L***	**M**	**L**	***H***	***M***	**L**	***M***	Y	Y	Y	Y	Y	Y	Y
Phosphoric acid, 1,3-phenylene tetraphenyl ester	57583-54-7	***L***	***L***	***L***	***L***	***L***	***M***	***L***	***L***	***H***	***L***	***M***	Y	Y	Y	N	Y	N	N
Phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester	98165-92-5	***L***	***L***	***L***	***L***	***L***	***M***	***L***	***L***	***L***	***L***	***L***	Y	Y	Y	N	Y	N	N
Triphenyl Phosphate	115-86-6	***L***	**L**	**L**	**L**	**L**	**M**	**L**	**H**	***H***	**L**	**L**	Y	Y	Y	Y	Y	Y	Y

Table 2-2 Definitions of Toxicological and Environmental Endpoints

Toxicological Category	Toxicological Endpoint	Definition
Human Health Effects	Cancer Hazard	Any malignant growth or tumor caused by abnormal and uncontrolled cell division.
	Skin Sensitizer	Chemical that causes an allergic skin reaction characterized by the presence of inflammation; may result in cell death.
	Reproductive	Adverse effects on the reproductive systems of females or males, including structural/functional alterations to the reproductive organs/system, the related endocrine system, mating, or fertility/reproductive success.
	Developmental*	Adverse effects on the developing organism (including structural abnormality, altered growth, or functional deficiency or death) resulting from exposure prior to conception (in either parent), during prenatal development, or postnatally up to the time of sexual maturation.
	Neurological	Adverse effects on the central or peripheral nervous system.
	Systemic	Adverse effect (other than those listed separately) that is of either a generalized nature or that occurs at a site distant from the point of entry of a substance: a systemic effect requires absorption and distribution of the substance in the body.
	Genotoxicity	Induction of genetic changes in a cell as a consequence of gene sequence changes (mutagenicity), or chromosome number/structure alterations.
Ecotoxicity	Adverse effects observed in living organisms (fish, birds, plants, etc.) that typically inhabit the wild.	
	Acute	Short-term, in relation to exposure or effect. Exposures are typically less than 96 hours.
	Chronic	Effects observed after repeated exposures.
Environmental	Persistence	Attribute of a substance that describes the length of time that the substance remains in the environment before it is physically removed by chemical or biological transformations.
	Bioaccumulation*	Ability of living organisms to concentrate a substance obtained either directly from the environment or indirectly through its food.

*REFERENCE: International Union of Pure and Applied Chemistry, Clinical Chemistry Division Commission on Toxicology. Glossary for Chemists of Terms Used in Toxicology (IUPAC Recommendations, 1993).

Each toxicological endpoint is assigned a rating of L, M, or H to indicate whether the chemical has a low (L), medium (M), or high (H) hazard concern. If the L, M, or H indicator is bold or colored, then the assignment was made using experimental data on the chemical. If the L, M, or H indicator is italicized, then experimental data were not available for that chemical and the assignment was estimated using modeling techniques and professional judgment. Similarly, each exposure route is assigned a rating of Y (yes) or N (no) to indicate whether that exposure route may occur for each chemical.

2.1 Explanation of Toxicological and Environmental Endpoints Rating

The assessments combine data on flame-retardant alternatives from three sources: (1) publicly available measured (experimental) data obtained from a comprehensive literature review; (2) estimations from EPA's New Chemical Program's P2 Framework and Sustainable Futures predictive methods; and (3) professional judgment of SRC staff who identified experimental data on closely related analogs. When experimental data were lacking, the expert judgment of scientists from Syracuse Research Corporation was used to assess physical/chemical property, environmental fate, aquatic toxicity and human health endpoints. The following abbreviations are used to indicate sources of data presented in this assessment:

- M = Measured/experimental data contained in the open literature;
- E = Estimations obtained using predictive methodology; and
- P = Professional judgment of subject matter experts.

Table 2-3 lists the criteria that were used to interpret the data collected in this document. These criteria are used by the EPA New Chemicals Program to assign concern levels to new chemicals submitted under the Toxic Substances Control Act (TSCA). EPA has published these criteria in several sources including USEPA 1992, USEPA 1994, and USEPA 1995. EPA New Chemicals Program persistence criteria have been published in the Federal Register (USEPA 1999a, 1999b).

Table 2-3 Criteria Used to Assign Concern Levels

Concern Level	Persistence Criteria
High	Half-life in water, soil, or sediment > 180 days
Moderate	Half-life in water, soil, or sediment between 60 and 180 days
Low	Half-life in water, soil, or sediment < 60 days
Concern Level	**Bioaccumulation Criteria**
High	Bioconcentration factor (BCF) > 5000
Moderate	BCF between 1,000 and 5,000
Low	BCF < 1,000
Concern Level *	**Aquatic Toxicity Criteria**
High	Value is ≤ 1 mg/L (chronic value <0.1 mg/L)
Moderate	Value is between 1 and 100 mg/L (chronic value 0.1 and 10 mg/L)
Low	Value is >100 mg/L (chronic value >10 mg/L) or log K_{ow} is greater than 8

Concern Level	Human Health Criteria
High	Evidence of adverse effects in human populations *or* conclusive evidence of severe effects in animal studies
Moderate	Suggestive animal studies, analog data, *or* chemical class known to produce toxicity
Low	No concern identified

*If the water solubility is estimated, the chemical will not be considered to have "no effects at saturation" if the estimated value is within a factor of 10 percent of the cutoff value. The concern level will be considered low if "no effects at saturation" (below the solubility limit).

More information on the EPA New Chemicals Program criteria used to assign concern levels can be found in the Sustainable Futures Pilot Project Interpretive Guidance Document available online at: http://www.epa.gov/oppt/newchems/sustainablefutures.htm.

If measured data pertaining to these criteria are not available, they can be estimated based on several physical and chemical properties. Estimations for these properties were obtained using the models of EPA's P2 Framework. The P2 Framework is an approach to risk-screening that incorporates pollution prevention principles in the design and development of chemicals. These models are screening level methods and are intended to be used when data are unavailable or to supplement available data. They are not intended to replace data from well-designed studies. For physical/chemical properties and environmental fate parameters, estimates were obtained from the Estimations Program Interface for Windows (EPIWIN) suite methodology. These methods were used to obtain melting point, boiling point, vapor pressure, octanol/water partition coefficient, water solubility, Henry's Law constant, atmospheric oxidation rate, biodegradation potential, soil adsorption coefficient, bioconcentration factor, hydrolysis rate, volatilization rates and removal in a sewage treatment plant as applicable. For aquatic toxicity potential, EPA's Ecological Structure Activity Relationships (ECOSAR) estimation program was used. This methodology uses chemical structure to estimate toxicity of an industrial chemical to fish, invertebrates, and algae in the surface water to which the chemical has been discharged. The program determines both acute (short-term) toxicity and, when available, chronic (long-term or delayed) toxicity. The potential for a chemical to cause cancer in humans was estimated using OncoLogic. This program uses a decision-tree based on the known carcinogenicity of chemicals with similar chemical structures, information on mechanisms of action, short-term predictive tests, epidemiological studies, and expert judgment.

The persistence of a chemical substance in a screening assessment is based on determining the importance of removal processes that may occur once a chemical enters the environment. As noted above, chemicals with a half-life of less than 60 days are expected to be of low concern for persistence based on the criteria that were used to interpret the data collected in this document. The persistence screening assessment does not directly address the pathways that a flame retardant might enter the environment (e.g.,

volatilization or disposal in a land fill) and focuses instead on the removal processes that are expected to occur once it is released to air, water, soil, or sediment. Determining how a chemical enters the environment is typically a component of a complete exposure assessment or life cycle analysis. Similarly, the persistence screening assessment does not address what might happen to a chemical substance throughout its life cycle, such as disposal during incineration of consumer or commercial products.

Environmental removal processes are generally divided into two categories: chemical and biological. One of the most important chemical degradation processes is hydrolysis. The importance of hydrolysis can be determined from experimental data (on both the compound of interest and closely related analogs) and by using the half-life obtained from the models within EPIWIN. Photolysis may also be an important environmental removal process and was considered in this assessment when experimental data were available. Estimation methods for photolysis are not available within EPA's Sustainable Futures pilot project.

In the absence of hydrolysis or other forms of chemical degradation, biodegradation is used to determine the persistence of a chemical substance in the environment. If experimental data on the biodegradation of a chemical substance are not available, then the potential of the chemical to undergo this process can be assessed from the results of the EPIWIN models. These models fall into three classes:

1. Probability of rapid biodegradation models based on linear and non-linear regressions that estimate the probability that a chemical substance will degrade fast;

2. Expert survey models – semi-quantitative models that determine the rate of ultimate and primary biodegradation; and

3. Probability of ready biodegradability.

The first set of models are useful for determining if a chemical substance has the potential to biodegrade quickly in the environment, but do not provide a quantitative indication of its half-life. If a chemical is likely to biodegrade quickly its half-life is expected to be less than 60 days and, therefore, it is expected to have a low concern for persistence. The results of the estimates from the first set of models are used in concert with the semi-quantitative output from the second set of models, which include an ultimate and primary survey model for evaluating persistence. These models provide a numeric result, ranging from 1 to 5, to provide an indication of the amount of time required for complete mineralization (ultimate degradation) and removal of the parent substance (primary degradation) of the test compound. The numeric result is converted to a more meaningful time frame for removal for the user based on the scheme presented in the following table. The results from the ultimate degradation model can also be used to estimate the half-life for a chemical, which is also provided in Table 2-4.

Table 2-4 Information for Estimating Biodegradation Half-Life

Model Results for Primary and Ultimate	Time for Removal	Approximate Half-Life (Days, Based on ultimate)
>4.75	Hours	0.17
4.75 to >4.25	Hours to Days	1.25
4.25 to >3.75	Days	2.33
3.75 to >3.25	Days to Weeks	8.67
3.25 to >2.75	Weeks	15
2.75 to >2.25	Weeks to Months	37.5
2.25 to >1.75	Months	60
#1.75	Recalcitrant	180

The third set of models (also known as MITI models), and the ready biodegradability test that they correspond to, are more applicable to determining a chemical's potential for removal in a sewage treatment plant than its persistence in the environment.

When determining environmental persistence, screening assessments also consider the potential persistence of metabolites resulting from biodegradation pathways and degradation products resulting from chemical removal processes. This assessment is performed because of the potential for human and environmental exposure to persistent degradation products or metabolites. Degradation products resulting from hydrolysis can be determined experimentally or by using professional judgment based on analogs with similar functional groups. Metabolism products may also be reported in experimental biodegradation tests or can be determined using professional judgment. When the rate for ultimate degradation is much slower than that for primary degradation, the potential for persistent metabolites exists.

2.2 Explanation of Exposure Route Rating

Six exposure routes are presented for each chemical, including two occupational exposure routes, three general population exposure routes and one aquatic exposure route. Each of these potential routes is assigned a Y (yes, exposure may occur) or an N (no, exposure is not likely to occur). The potential for occupational exposure is determined by the physicochemical properties of the pure material. The thresholds for each exposure route were adapted from EPA's New Chemicals Program, except as noted.

Occupational Exposure

Inhalation

Liquids[1]: If a liquid has a vapor pressure amenable to volatilization, then the liquid will evaporate and present the potential for a person to inhale the vapor. Occupational

[1] Liquids are substances that have a melting point less than 25 degrees Celsius and a boiling point greater than 25 degrees Celsius.

exposure may occur when the vapor pressure is greater than 1 x 10^{-06} mm Hg at 25 degrees Celsius. Liquids may also be inhaled as a mist if the liquid chemical is sprayed during transfer or application operations.

Solids[2]: Occupational exposure may occur in all cases when processing or handling solids. Solid-state chemicals may be used in a crystalline, packed, or powder form. In all cases, a solid chemical may produce particulate dust as a byproduct of manufacturing or use operations. When this occurs, a worker may inhale the dust particles while working with the chemical.

Gases[3]: Occupational exposure may occur in all cases when processing or handling gases. Gaseous chemicals should always be contained in cylinders to enable their use; however, if they are uncontained, gaseous chemicals result in exposure to workers. Routine exposure to gaseous chemicals is not expected unless there is an accident. However, fugitive releases may occur when connecting transfer lines.

Dermal

Dermal exposures may occur to workers while handling liquid or solid flame-retardant chemicals. In general, workers handling liquid chemicals may be exposed to the chemical by full hand immersion, splashing, or spraying depending upon the manufacturing processes utilized at a facility. Workers handling solid chemicals can be exposed on the surface of their hands as well as from particulate dust that may settle onto their skin. All chemicals are expected to present a dermal exposure to workers in this report. The use of personal protective equipment may mitigate these exposures.

Ingestion

Exposures associated with ingestion are not included for the purposes of this screening level assessment; however, workers may incidentally ingest flame-retardant chemicals through ingestion of contaminated food and water. Ingestion may occur if the chemical is suspended in air as a particulate or a mist as part of manufacturing, and then recondenses or flocculates into food or drinking sources. Alternatively, secondary ingestion may occur as a result of inhaling the mist or dust form of the chemical, and then swallowing residual chemical in the nasal or esophageal passageways.

General Population Exposure

Inhalation

Liquids[4]: If the liquid has a vapor pressure amenable to volatilization from the product in which the chemical is carried, a person may inhale the liquid as a vapor while in contact

[2] Solids are substances that have a melting point of greater than 25 degrees Celsius.
[3] Gases are substances that have a boiling point less than 25 degrees Celsius.
[4] Liquids are substances that have a melting point less than 25 degrees Celsius and a boiling point greater than 25 degrees Celsius.

with the product or substance carrying the chemical. For this report, general population exposure may occur if the chemical vapor pressure is greater than 1 x 10^{-06} mm Hg at 25 degrees Celsius and if the chemical is additive, not reactive[5].

Solids[6]: General population exposure may occur if the vapor pressure is greater than 1 x 10^{-06} mm Hg at 25 degrees Celsius and if the chemical is not reactive. Although not included in this screening level assessment, as products age and break down, particulate (matter) may be released from the products which may contain flame-retardant chemicals. This flame-retardant dust could represent an exposure to the general population.

Gases[7]: General population exposure is not expected to occur if the chemical is a gas, since gases would not be intentionally contained outside of the manufacturing arena (excluding accidental releases).

Dermal

Dermal exposures may occur to the general population while handling products or substances containing the flame-retardant chemical, if the flame-retardant chemical is not reactive.

Ingestion

The general population may be exposed to a flame-retardant chemical if the chemical has water solubility greater than 1 x 10^{-06} grams/liter, is dispersible, or has the potential to leach. These would indicate that the chemical is easily absorbed in water and may be found in surface and groundwater sources as a result of disposal and environmental releases of the chemical.

Aquatic Exposure

The flame-retardant chemical may present an aquatic exposure if the water solubility of the compound is greater than 1 x 10^{-06} grams/liter or the compound is dispersible in water.

[5] Reactive chemicals (as opposed to additive chemicals) are those that are incorporated into the foam by new chemical bonds that are formed between the substrate and the flame retardant. Therefore, they are not assumed to be available for exposure.
[6] Solids are substances that have a melting point of greater than 25 degrees Celsius.
[7] Gases are substances that have a boiling point less than 25 degrees Celsius.

References

U.S. EPA. 1992. Classification Criteria for Environmental Toxicity and Fate of Industrial Chemicals. Office of Prevention, Pesticides and Toxics (OPPT), Chemical Control Division (CCD), 401 M. St. SW, Washington, DC 20460.

U.S. EPA. 1994. US EPA/EC Joint Project on the Evaluation of (Quantitative) Structure Activity Relationships. Office of Prevention, Pesticides and Toxic Substances, Washington, DC 20460. March 1994. EPA 743-R-94-001. http://www.epa.gov/oppt/newchems/21ecosar.htm

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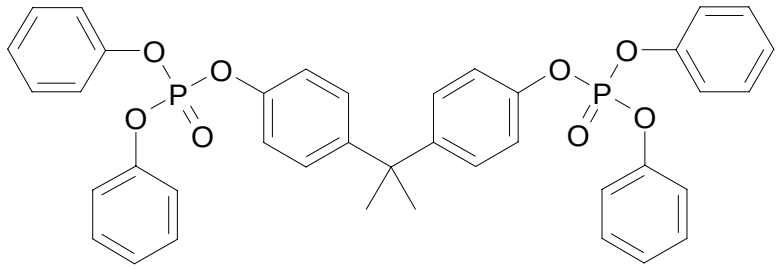
U.S. EPA. 1999a. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances, Federal Register: November 4, 1999 (Volume 64, Number 213), pages 60194-60204 Available at: http://www.epa.gov/fedrgstr/EPA-TOX/1999/November/Day-04/t28888.htm

U.S. EPA. 1999b. Persistent Bioaccumulative Toxic (PBT) Chemicals; Lowering of Reporting Thresholds for Certain PBT Chemicals; Addition of Certain PBT Chemicals; Community Right-to-Know Toxic Chemical Reporting: Final rule, Federal Register: October 29, 1999 (Volume 64, Number 209), 58666-58753 Available in PDF at: http://www.epa.gov/tri/pbt-final_rule.pdf

3.0 Chemical Summary Assessments

The following section contains summaries of the toxicity and exposure data for 5 chemicals that are components of the flame retardant formulations assessed in this report. These summary data were used to develop the hazard concern and exposure conclusions that are presented in Table 2-1. The studies from which these data were derived are summarized in Section 4.0 of this report, entitled Chemical Hazard Reviews.

Record ID **WS-1** Bisphenol A bis(diphenyl phosphate)	**CAS No.** 5945-33-5
	**MW**: 692.65
	MF: $C_{39}H_{34}O_8P_2$
	Physical Forms: **Neat:** Solid **As Formulated:** Liquid
	Use: Flame retardant, additive
SMILES: c1ccccc1OP(Oc2ccccc2)(=O)Oc3ccc(cc3)C(C)(C)c4ccc(cc4)OP(=O)(Oc5ccccc5)(Oc6ccccc6)	
Name: Phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester	
Synonyms: Bisphenol A bis(diphenyl phosphate); BAPP; BDP	

ASSESSMENT SUMMARY:

	Concern Level		
	HIGH	**MODERATE**	**LOW**
Persistence	**X**		
Bioconcentration			**X**
Cancer Health Hazard			**X**
Non-Cancer Health Hazard		**X***	
Aquatic Toxicity Hazard			**X**
Is the chemical predicted to be a PBT by PBT Profiler?	**No**		
Overall Hazard Concern	**Human Health Hazard: Moderate** **Aquatic Hazard: Low**		

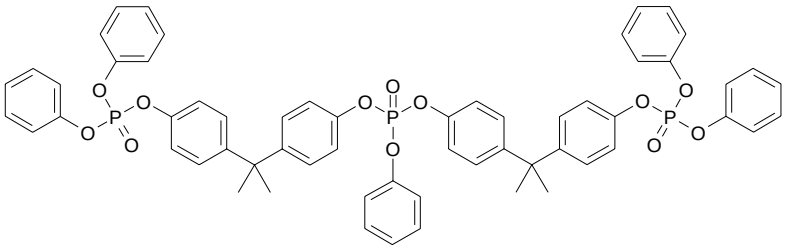
* Based on systemic effects (for analog, triphenyl phosphate) and eye irritation (for analog and mixtures containing 5945-33-5 as major component)

Record ID: WS-1	**CAS No.** 5945-33-5
PHYSICAL/CHEMICAL PROPERTIES	
Melting Point (deg C)	90 (E)
Boiling Point (deg C)	>400 (E)
Vapor Pressure (mm Hg)	$<10^{-6}$ (E)
Water Solubility (g/L)	$<10^{-6}$ (E)
Log K_{ow}	10.0 (E)
ENVIRONMENTAL TRANSPORT AND FATE:	
Transport	
Henry's Law Constant – HLC (atm-m^3/mole)	$5x10^{-14}$ (E)
Soil Adsorption Coefficient – K_{oc}	$1x10^{10}$ (E)
Bioconcentration Factor – BCF	3 (E)
Persistence	
Experimental Biodeg Tests	2% CO_2 evolution from sandy loam and associated natural waters and 3% CO_2 evolution from sandy silt loam and associated natural waters over 180 days, 77% and 72% recovery of original material at day 180; 2% biodegradation in 28 days in sewage sludge; 3-6% biodegradation in 28 days in sewage sludge; 21.5% biodegradation in 29 days in activated sludge (M, for mixture 181028-79-5)
Ultimate Biodeg Model	Months (E)
Primary Biodeg Model	Days-Weeks (E)
BOD or COD	
Atmospheric Half-life	5.5 hours for gas phase reaction (E); Extremely low percentage of compound is in the gas phase (P)
Hydrolysis Half-life	
Volatilization Half-life for Model River	Negligible (E)
Volatilization Half-life for Model Lake	Negligible (E)
Removal in Sewage Treatment Plant	97% by adsorption to sludge (E)

Record ID: WS-1	CAS No. 5945-33-5
Ready Biodegradability	Not Ready Biodegradable (E)
Byproducts	
Degradation Products	Phenol, Bisphenol A
Metabolites	
ECOTOXICITY:	
ECOSAR Class	Esters (phosphate), Esters
Comments	
Acute Toxicity	
Fish LC_{50}	96-h LC50, NES (No effects at saturation) (E)
Daphnid LC_{50}	48-h LC50, NES (E)
Green Algae EC_{50}	96-h EC50, NES (E)
Chronic Toxicity	
Fish ChV	NES (E)
Daphnid ChV	NES (E)
Green Algae ChV	NES (E)
Overall Hazard Concern for Aquatic Toxicity	LOW
HEALTH EFFECTS:	
Absorption	Poor through GI tract based on results for mixture 181028-79-5 (M,P)
CANCER HEALTH EFFECTS:	
Experimental data	
OncoLogic Results	Structure could not be evaluated due to absence of relevant fragments in OncoLogic
Overall Hazard Concern for Carcinogenicity	LOW by analogy to triphenyl phosphate
NON-CANCER HEALTH EFFECTS:	
Acute Toxicity	Low by analogy to triphenyl phosphate: Rat, mouse, rabbit, oral, LD50 > 5000 mg/kg; rabbit, dermal, LD50 > 7900 mg/kg (P); also by results for mixtures 181028-79-5: rat, oral LD50 > 5000 mg/kg; rabbit, dermal, LD50 > 2000 mg/kg (M,P)

Record ID: WS-1	**CAS No.** 5945-33-5
Eye Irritation	Moderate by analogy to triphenyl phosphate: Mild eye irritation, rabbits (P); also by results for mixtures 181028-79-5: Minimal eye irritation, rabbits (M,P)
Skin Irritation	Low by analogy to triphenyl phosphate: Negative, rabbits (P); also by results for mixtures 181028-79-5: Negative (2 studies) or slight (2 studies), 4-hr, rabbits; Negative (3 studies) or slight (1 study), 24-hr, rats (M, P)
Skin Sensitizer	Low by analogy to triphenyl phosphate: very low incidence in humans (P); also by results for mixtures 181028-79-5: Negative, guinea pig (M, P)
Reproductive Effects	Low by analogy to triphenyl phosphate: Negative in 91-112-d reproductive (incomplete)/developmental study, rats, diet, NOAEL = 690 mg/kg/day (1%) (P)
Developmental Effects	Low by analogy to triphenyl phosphate: Negative in 91-112-d reproductive-developmental study, rats, diet, NOAEL = 690 mg/kg/day (1%) (P); also by results for mixture 181028-79-5: Negative in 14-d developmental study, rats, oral gavage, NOAEL = 1000 mg/kg/day (M,P)
Immune System Effects	Low by analogy to triphenyl phosphate: Negative in 120-d repeated-dose study, rats, diet, NOAEL = 700 mg/kg/day (1%) (P)
Neurotoxicity	Low by analogy to triphenyl phosphate: Negative in delayed neurotoxicity studies in hen at ≤10,000 mg/kg/day (oral, 6 dosing days) and cat at 700 mg/kg (subcutaneous, single dose); Negative in120-d repeated-dose neurotoxicity screening study, rats, diet, NOAEL = 711 mg/kg/day (1.0%) (P); also by results for mixture 181028-79-5: 28-d repeated-dose study, rats, oral gavage, no neurobehavioral effects (assayed weekly), NOAEL = 1000 mg/kg/day (M,P)

Record ID: WS-1	**CAS No.** 5945-33-5
Genotoxicity/Mutagenicity	Low by analogy to triphenyl phosphate: Negative with and without metabolic activation in Ames assay, in forward mutation assay (mouse lymphoma cells *in vitro),* and in mitotic gene conversion assay (*Saccharomyces cerevisiae)* (P); also by results for mixtures 181028-79-5: Negative with or without metabolic activation in Ames assays, chromosomal aberration assays *in vitro* (human lymphocytes; Chinese hamster lung or ovary cells), and in mouse bone marrow micronucleus assays, oral, gavage, NOAEL = 2000 mg/kg, and intraperitoneal injection, NOAEL = 5000 mg/kg (M, P)
Systemic Effects	Moderate by analogy to triphenyl phosphate: 35-d repeated-dose study (inadequate), rats, diet, increased relative liver weight at 0.5%, NOAEL = 0.1%; 120-d repeated-dose (neurotoxicity screening) study, rats, diet, decreased body weight gain without decreased food consumption, NOAEL = 161 mg/kg/day (0.25%), LOAEL = 345 mg/kg/day (1%); 21-d repeated-dose study (inadequate), rabbits, dermal, systemic effects (P); Low by results for mixtures 181028-79-5: 28-d repeated-dose studies, rats, oral gavage, no adverse effects, NOAEL = 1000 mg/kg/day; 28-day repeated-dose study, rats, diet, no adverse effects, 20,000 ppm, NOAEL = 1862 mg/kg/day (males) and 1968 mg/kg/day (females) (M,P)
Overall Hazard Concern for Non-Cancer Health Effects	MODERATE

Record ID WS-2 Phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester	**CAS No.** 83029-72-5
	**MW**: 1059.00
	MF: $C_{60}H_{53}O_{12}P_3$
	Physical Forms: **Neat:** Solid **As Formulated:** Liquid
	Use: Flame retardant, additive
SMILES: c1ccccc1OP(Oc2ccccc2)(=O)Oc3ccc(cc3)C(C)(C)c4ccc(cc4)OP(=O)(Oc5ccccc5)Oc6ccc(cc6)C(C)(C)c7ccc(cc7)OP(=O)(Oc8ccccc8)Oc9ccccc9	
Name: Phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester	
Synonyms:	

ASSESSMENT SUMMARY:

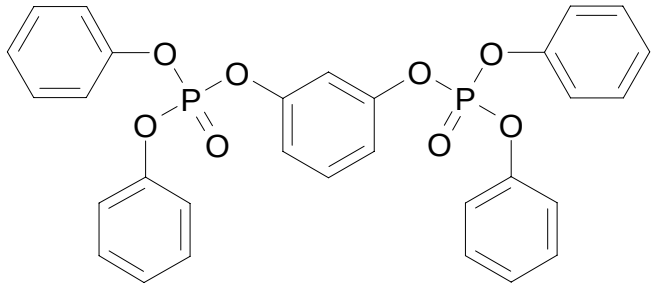
	Concern Level		
	HIGH	**MODERATE**	**LOW**
Persistence	**X**		
Bioconcentration			**X**
Cancer Health Hazard			**X**
Non-Cancer Health Hazard		**X***	
Aquatic Toxicity Hazard			**X**
Is the chemical predicted to be a PBT by PBT Profiler?	**NA**		
Overall Hazard Concern	**Human Health Hazard: Moderate** **Aquatic Hazard: Low**		

* Based on systemic effects and eye irritation for analog, triphenyl phosphate.

Record ID: WS-2	**CAS No.** 83029-72-5
PHYSICAL/CHEMICAL PROPERTIES	
Melting Point (deg C)	90 (E)
Boiling Point (deg C)	>400 (E)
Vapor Pressure (mm Hg)	$<10^{-6}$ (E)
Water Solubility (g/L)	$<10^{-6}$ (E)
Log K_{ow}	>10 (E)
ENVIRONMENTAL TRANSPORT AND FATE:	
Transport	
Henry's Law Constant – HLC (atm-m^3/mole)	$5x10^{-14}$ (E)
Soil Adsorption Coefficient – K_{oc}	$1x10^{10}$ (E)
Bioconcentration Factor – BCF	3 (E)
Persistence	
Experimental Biodeg Tests	2% CO_2 evolution from sandy loam and associated natural waters and 3% CO_2 evolution from sandy silt loam and associated natural waters over 180 days, 77% and 72% recovery of original material at day 180; 2% biodegradation in 28 days in sewage sludge; 3-6% biodegradation in 28 days in sewage sludge; 21.5% biodegradation in 29 days in activated sludge (M, for mixture 181028-79-5)
Ultimate Biodeg Model	Recalcitrant (E)
Primary Biodeg Model	Days-Weeks (E)
BOD or COD	
Atmospheric Half-life	3.5 Hours for gas phase reaction (E); Extremely low percentage of compound is in the gas phase (P)
Hydrolysis Half-life	
Volatilization Half-life for Model River	Negligible (E)
Volatilization Half-life for Model Lake	Negligible (E)
Removal in Sewage Treatment Plant	94% (E)

Record ID: WS-2	**CAS No.** 83029-72-5
Ready Biodegradability	Not Ready Biodegradable (E)
Byproducts	
Degradation Products	Phenol, Bisphenol A
Metabolites	
ECOTOXICITY:	
ECOSAR Class	Esters (phosphate), Esters
Comments	
Acute Toxicity	
Fish LC_{50}	96-h LC50, NES (No effects at saturation) (E)
Daphnid LC_{50}	48-h LC50, NES (E)
Green Algae EC_{50}	96-h EC50, NES (E)
Chronic Toxicity	
Fish ChV	NES (E)
Daphnid ChV	NES (E)
Green Algae ChV	NES (E)
Overall Hazard Concern for Aquatic Toxicity	LOW
HEALTH EFFECTS:	
Absorption	Low throught GI tract, lung, poor through skin because of molecular size (P)
CANCER HEALTH EFFECTS:	
Experimental data	
OncoLogic Results	Structure could not be evaluated due to absence of relevant fragments in OncoLogic
Overall Hazard Concern for Carcinogenicity	LOW by analogy to triphenyl phosphate (P)
NON-CANCER HEALTH EFFECTS:	
Acute Toxicity	Low by analogy to triphenyl phosphate; Rat, mouse, rabbit, oral, LD50 > 5000 mg/kg; rabbit, dermal, LD50 > 7900 mg/kg (P)
Eye Irritation	Moderate by analogy to triphenyl phosphate; Mild eye irritation, rabbits (P)

Record ID: WS-2	**CAS No.** 83029-72-5
Skin Irritation	Low by analogy to triphenyl phosphate; Negative, rabbits (P)
Skin Sensitizer	Low by analogy to triphenyl phosphate; very low incidence in humans (P)
Reproductive Effects	Low by analogy to triphenyl phosphate; Negative in 91-112-d reproductive (incomplete)/developmental study, rats, diet, NOAEL = 690 mg/kg/day (1%) (P)
Developmental Effects	Low by analogy to triphenyl phosphate; Negative in 91-112-d reproductive-developmental study, rats, diet, fetal and maternal NOAELs = 690 mg/kg/day (1%)(P)
Immune System Effects	Low by analogy to triphenyl phosphate; Negative in 120-d repeated-dose study, rats, diet, NOAEL = 700 mg/kg/day (1%) (P)
Neurotoxicity	Low by analogy to triphenyl phosphate; Negative in delayed neurotoxicity studies in hen at ≤10,000 mg/kg/day (oral, 6 dosing days) and in cat at 700 mg/kg (subcutaneous, single dose) and in 120-d repeated-dose neurotoxicity screening study, rats, diet, NOAEL = 711 mg/kg/day (1.0%) (P)
Genotoxicity/Mutagenicity	Low by analogy to triphenyl phosphate; Negative with and without metabolic activation in Ames assay, in forward mutation assay (mouse lymphoma cells *in vitro*), and in mitotic gene conversion assay (*Saccharomyces cerevisiae*) (P)
Systemic Effects	Moderate by analogy to triphenyl phosphate; 35-d repeated-dose study (inadequate), rats, diet, increased relative liver weight at 0.5%, NOAEL = 0.1%; 120-d repeated-dose (neurotoxicity screening) study, rats, diet, decreased body weight gain without decreased food consumption, NOAEL = 161 mg/kg/day (0.25%), LOAEL = 345 mg/kg/day (1%); 21-d repeated-dose study (inadequate), rabbits, dermal, systemic effects (P)
Overall Hazard Concern for Non-Cancer Health Effects	MODERATE

Record ID WS-3 Resorcinol bis(diphenylphosphate)	**CAS No.** 57583-54-7
	**MW**: 574.47
	MF: $C_{30}H_{24}O_8P_2$
	Physical Forms: **Neat:** Solid **As Formulated:** Liquid
	Use: Flame retardant, additive
SMILES: c1ccccc1OP(Oc2ccccc2)(=O)Oc3cccc(c3)OP(=O)(Oc4ccccc4)Oc5ccccc5	
Name: Phosphoric acid, 1,3-phenylene tetraphenyl ester	
Synonyms: Resorcinol bis(diphenylphosphate); RBDPP; RDP	

ASSESSMENT SUMMARY:

	Concern Level		
	HIGH	**MODERATE**	**LOW**
Persistence			**X**
Bioconcentration		**X**	
Cancer Health Hazard			**X**
Non-Cancer Health Hazard		**X***	
Aquatic Toxicity Hazard	**X**		
Is the chemical predicted to be a PBT by PBT Profiler?	**No**		
Overall Hazard Concern	**Human Health Hazard: Moderate** **Aquatic Hazard: High**		

* Based on eye irritation and systemic effects (for analog triphenyl phosphate and mixtures containing 57583-54-7 as a major component)

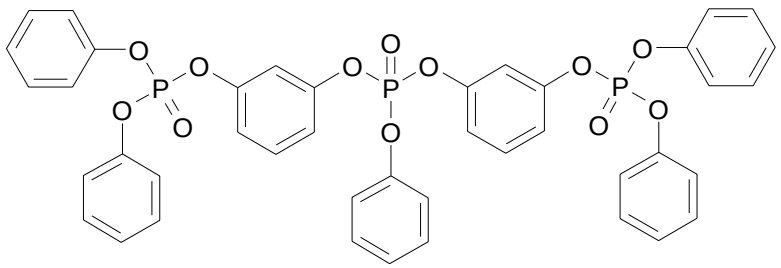
Record ID: WS-3	**CAS No.** 57583-54-7
PHYSICAL/CHEMICAL PROPERTIES	
Melting Point (deg C)	90 (E)
Boiling Point (deg C)	>400 (E)
Vapor Pressure (mm Hg)	$<10^{-6}$ (E)
Water Solubility (g/L)	$<10^{-6}$ (E)
Log K_{ow}	7.41 (E)
ENVIRONMENTAL TRANSPORT AND FATE:	
Transport	
Henry's Law Constant – HLC (atm-m^3/mole)	$3x10^{-13}$ (E)
Soil Adsorption Coefficient – K_{oc}	$1x10^{8}$ (E)
Bioconcentration Factor – BCF	3000 (E)
Persistence	
Experimental Biodeg Tests	
Ultimate Biodeg Model	Weeks-Months (E)
Primary Biodeg Model	Days (E)
BOD or COD	
Atmospheric Half-life	6.1 hours for gas phase reaction (E); Extremely low percentage of compound is in the gas phase (P)
Hydrolysis Half-life	Half-life at 20 °C: 11 days at pH 4; 17 days at pH 7; 21 days at pH 9 (M, for mixture 125997-21-9)
Volatilization Half-life for Model River	Negligible (E)
Volatilization Half-life for Model Lake	Negligible (E)
Removal in Sewage Treatment Plant	99% (E)
Ready Biodegradability	Not Ready Biodegradable (E)
Byproducts	
Degradation Products	Phenol, resorcinol
Metabolites	

Record ID: WS-3	CAS No. 57583-54-7
ECOTOXICITY:	
ECOSAR Class	Esters (phosphate), esters
Comments	
Acute Toxicity	
Fish LC_{50}	96-h LC50, NES (No effects at saturation) (E)
Daphnid LC_{50}	48-h LC50, NES (E)
Green Algae EC_{50}	96-h EC50, NES (E)
Chronic Toxicity	
Fish ChV	0.001 mg/L (E)
Daphnid ChV	0.0005 mg/L (Acute/chronic ratio=10, E)
Green Algae ChV	NES (E)
Overall Hazard Concern for Aquatic Toxicity	HIGH (chronic toxicity only)
HEALTH EFFECTS:	
Absorption	Moderate through lungs, low through GI tract and poor through skin (M)
CANCER HEALTH EFFECTS:	
Experimental data	
OncoLogic Results	Structure could not be evaluated due to absence of relevant fragments in OncoLogic
Overall Hazard Concern for Carcinogenicity	LOW by analogy to triphenyl phosphate
NON-CANCER HEALTH EFFECTS:	
Acute Toxicity	Low by analogy to triphenyl phosphate: Rat, mouse, rabbit, oral, LD50 > 5000 mg/kg; rabbit, dermal, LD50 > 7900 mg/kg (P); also by results for mixtures 125997-21-9: rat, oral, LD50 > 5000 mg/kg; rat, dermal, LD50 > 2000 mg/kg; rat, inhalation, labored respiration at 4680 mg/m^3, LC50 > 4860 mg/m^3 (M,P)
Eye Irritation	Moderate by analogy to triphenyl phosphate: Mild eye irritation, rabbits (P); also by results for mixture 125997-21-9: Minimal eye irritation, rabbits (M,P)

Record ID: WS-3	**CAS No.** 57583-54-7
Skin Irritation	Low by analogy to triphenyl phosphate: Negative, rabbits (P); also by results for mixture 125997-21-9: Negative, rabbits (M,P)
Skin Sensitizer	Low by analogy to triphenyl phosphate: very low incidence in humans (P); also by results for mixture 125997-21-9: Negative, guinea pig (M,P)
Reproductive Effects	Low by analogy to triphenyl phosphate; Negative in 91-112-d reproductive (incomplete)/ developmental study, rats, diet, NOAEL = 690 mg/kg/day (1%) (P); also by results for mixture 125997-21-9: 112-d two-generation reproductive study, rats, diet, no effects on reproduction, sperm or estrus parameters at 20,000 ppm, NOAEL = 1203 mg/kg/day for males and 1305 mg/kg/day for females (M,P)
Developmental Effects	Low by analogy to triphenyl phosphate: Negative in 91-112-d reproductive-developmental study, rats, diet, fetal/maternal NOAEL = 690 mg/kg/day, (1%) (P); also by results for mixture 125997-21-9: Negative in 23-d developmental study, rabbits, oral gavage, NOAEL = 1000 mg/kg/day (M,P)
Immune System Effects	Low by analogy to triphenyl phosphate: 120-d repeated-dose study, rats, diet, no immune system effects, NOAEL = 700 mg/kg/day (1%) (P)); also by results for mixture 125997-21-9: Negative in 28-day immunotoxicity study, mice, oral gavage, NOAEL = 5000 mg/kg/day (M,P)

Record ID: WS-3	**CAS No.** 57583-54-7
Neurotoxicity	Low by analogy to triphenyl phosphate: Negative in delayed neurotoxicity studies in hen at ≤10,000 mg/kg/day (oral, 6 dosing days) and in cat at 700 mg/kg (subcutaneous, single dose); Negative in120-d repeated-dose neurotoxicity screening study, rats, diet, NOAEL = 711 mg/kg/day (1.0%) (P); also by results for mixtures 125997-21-9: no neurotoxicity-related clinical signs in acute oral gavage assays, rats, NOAEL = 5000 mg/kg or in 28-d repeated-dose oral gavage assay, rats, NOAEL = 1000 mg/kg/day (M,P
Genotoxicity/Mutagenicity	Low by analogy to triphenyl phosphate: Negative with and without activation in Ames assay, in forward mutation assay (mouse lymphoma cells *in vitro*), and in mitotic gene conversion assay (*Saccharomyces cerevisiae*) (P); also by results for mixtures 125997-21-9: Negative with or without metabolic activation in Ames assays, in chromosomal aberration assays in vitro (human lymphocytes), and in bone marrow micronucleus assay, mice, oral gavage, NOAEL = 5000 mg/kg (M,P)

Record ID: WS-3	**CAS No.** 57583-54-7
Systemic Effects	Moderate by analogy to triphenyl phosphate: 35-d repeated-dose study (inadequate), rats, diet, increased relative liver weight at 0.5%, NOAEL = 0.1%; 120-d repeated-dose (neurotoxicity screening) study, rats, diet, decreased body weight gain without decreased food consumption, NOAEL = 161 mg/kg/day (0.25%), LOAEL = 345 mg/kg/day (1%); 21-d repeated-dose study (inadequate), rabbits, dermal, systemic effects (P); also by results for mixtures 125997-21-9: 28-d repeated dose inhalation assay, rats, lung histopathology (alveolar histiocytosis), NOAEL = 100 mg/m^3, LOAEL = 500 mg/m^3 (at 2000 mg/m^3, lung developed chronic inflammation during 60-d post-exposure period; 28-d repeated-dose assay, rats, oral gavage, NOAEL = 1000 mg/kg/day;); 28-d immunotoxicity assay, rats, oral gavage, no effects on body weight, NOAEL = 5000 mg/kg/day; 112-d reproductive toxicity assay, rat, diet, no treatment-related adverse effect on body weight or liver at 20,000 ppm, NOAEL = 1203 mg/kg/day for males and 1305 mg/kg/day for females (M,P)
Overall Hazard Concern for Non-Cancer Health Effects	MODERATE

Record ID WS-4 Phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester	**CAS No.** 98165-92-5
	**MW**: 822.64
	MF: $C_{42}H_{33}O_{12}P_3$
	Physical Forms: **Neat:** Solid **As Formulated:** Liquid
	Use: Flame retardant, additive
SMILES: c1ccccc1OP(Oc2ccccc2)(=O)Oc3cccc(c3)OP(=O)(Oc4ccccc4)Oc5cccc(c5)OP(=O)(Oc6ccccc6)Oc7ccccc7	
Name: Phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester	
Synonyms:	

ASSESSMENT SUMMARY:

	Concern Level		
	HIGH	**MODERATE**	**LOW**
Persistence			**X**
Bioconcentration			**X**
Cancer Health Hazard			**X**
Non-Cancer Health Hazard		**X***	
Aquatic Toxicity Hazard			**X**
Is the chemical predicted to be a PBT by PBT Profiler?	**No**		
Overall Hazard Concern	**Human Health Hazard: Moderate** **Aquatic Hazard: Low**		

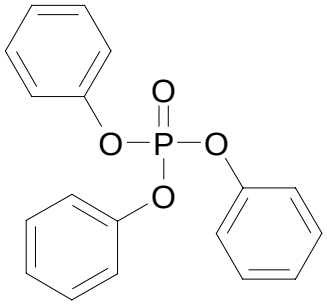
* Based on eye irritation and systemic effects (for analog triphenyl phosphate and mixtures containing 98165-92-5 as a minor component)

Record ID: WS-4	**CAS No.** 98165-92-5
PHYSICAL/CHEMICAL PROPERTIES	
Melting Point (deg C)	90 (E)
Boiling Point (deg C)	>400 (E)
Vapor Pressure (mm Hg)	$<10^{-6}$ (E)
Water Solubility (g/L)	$<10^{-6}$ (E)
Log K_{ow}	10.1 (E)
ENVIRONMENTAL TRANSPORT AND FATE:	
Transport	
Henry's Law Constant – HLC (atm-m^3/mole)	$2x10^{-18}$ (E)
Soil Adsorption Coefficient – K_{oc}	$1x10^{10}$ (E)
Bioconcentration Factor – BCF	3 (E)
Persistence	
Experimental Biodeg Tests	
Ultimate Biodeg Model	Months (E)
Primary Biodeg Model	Days (E)
BOD or COD	
Atmospheric Half-life	4.1 hours for gas phase reaction (E); Extremely low percentage of compound is in the gas phase (P)
Hydrolysis Half-life	Half-life at 20 °C: 11 days at pH 4; 17 days at pH 7; 21 days at pH 9 (M, for mixture 125997-21-9)
Volatilization Half-life for Model River	Negligible (E)
Volatilization Half-life for Model Lake	Negligible (E)
Removal in Sewage Treatment Plant	98% (E)
Ready Biodegradability	Not Ready Biodegradable (E)
Byproducts	
Degradation Products	Phenol, resorcinol
Metabolites	

Record ID: WS-4	CAS No. 98165-92-5
ECOTOXICITY:	
ECOSAR Class	Esters (phosphate), Esters
Comments	
Acute Toxicity	
Fish LC_{50}	96-h LC50, NES (No effects at saturation) (E)
Daphnid LC_{50}	48-h LC50, NES (E)
Green Algae EC_{50}	96-h EC50, NES (E)
Chronic Toxicity	
Fish ChV	NES (E)
Daphnid ChV	NES (E)
Green Algae ChV	NES (E)
Overall Hazard Concern for Aquatic Toxicity	LOW
HEALTH EFFECTS:	
Absorption	Likely to be low-to-poor by all routes based on analogy to the smaller resorcinol bis(diphenyl phosphate) (57583-54-7) (P)
CANCER HEALTH EFFECTS:	
Experimental data	
OncoLogic Results	Structure could not be evaluated due to absence of relevant fragments in OncoLogic
Overall Hazard Concern for Carcinogenicity	LOW by analogy to triphenyl phosphate
NON-CANCER HEALTH EFFECTS:	
Acute Toxicity	Low by analogy to triphenyl phosphate; Rat, mouse, rabbit, oral, LD50 > 5000 mg/kg; rabbit, dermal, LD50 > 7900 mg/kg (P); also by results for mixtures 125997-21-9: rat, inhalation, labored respiration at 4680 mg/m^3, LC50 > 4860 mg/m^3; Although only a minor component, 98165-92-5 is expected to contribute to lung effects; LC50 value may be an underestimate for pure 98165-92-5 (M,P)
Eye Irritation	Moderate by analogy to triphenyl phosphate; Mild eye irritation, rabbits (P)

Record ID: WS-4	**CAS No.** 98165-92-5
Skin Irritation	Low by analogy to triphenyl phosphate; Negative, rabbits (P)
Skin Sensitizer	Low by analogy to triphenyl phosphate; very low incidence in humans (P)
Reproductive Effects	Low by analogy to triphenyl phosphate; Negative in 91-112-d reproductive (incomplete)/developmental study, rats, diet, NOAEL = 690 mg/kg/day (1%) (P)
Developmental Effects	Low by analogy to triphenyl phosphate; Negative in 91-112-d reproductive-developmental study, rats, diet, fetal and maternal NOAELs = 690 mg/kg/day (1%) (P)
Immune System Effects	Low by analogy to triphenyl phosphate; 120-d repeated-dose study, rats, diet, no immune system effects, NOAEL = 700 mg/kg/day (1%) (P)
Neurotoxicity	Low by analogy to triphenyl phosphate; Negative in delayed neurotoxicity studies in hen at ≤10,000 mg/kg/day (oral, 6 dosing days) and cat at 700 mg/kg (subcutaneous, single dose); Negative in 120-d repeated-dose neurotoxicity screening study, rats, diet, NOAEL = 711 mg/kg/day (1.0%) (P)
Genotoxicity/Mutagenicity	Low by analogy to triphenyl phosphate; Negative with and without activation in Ames assay, in forward mutation assay (mouse lymphoma cells *in vitro*), and in mitotic gene conversion assay (*Saccharomyces cerevisiae)* (P)

Record ID: WS-4	**CAS No.** 98165-92-5
Systemic Effects	Moderate by analogy to triphenyl phosphate; 35-d repeated-dose study (inadequate), rats, diet, increased relative liver weight at 0.5%, NOAEL = 0.1%; 120-d repeated-dose (neurotoxicity screening) study, rats, diet, decreased body weight gain without decreased food consumption, NOAEL = 161 mg/kg/day (0.25%), LOAEL = 345 mg/kg/day (1%); 21-d repeated-dose study (inadequate), rabbits, dermal, systemic effects (P); also by results for mixtures 125997-21-9: 28-d repeated dose inhalation assay, rats, lung histopathology (alveolar histiocytosis), NOAEL = 100 mg/m^3, LOAEL = 500 mg/m^3 (at 2000 mg/m^3, lung developed chronic inflammation during 60-d post-exposure period); Although only a minor component, 98165-92-5 is expected to contribute to lung pathology, hence the LOAEL is an underestimate for pure 98165-92-5 (M, P)
Overall Hazard Concern for Non-Cancer Health Effects	MODERATE

Record ID: WS-5 Triphenyl Phosphate	**CAS No.** 115-86-6
	**MW**: 326.29
	MF: $C_{18}H_{15}O_4P$
	Physical Forms: **Neat:** Solid **As Formulated:** Liquid
	Use: Flame retardant, additive
SMILES: c1ccccc1OP(=O)(Oc2ccccc2)Oc3ccccc3	
Name: Phosphoric acid, triphenyl ester	
Synonyms: Triphenyl phosphate; TPP	

ASSESSMENT SUMMARY:

	Concern Level		
	HIGH	**MODERATE**	**LOW**
Persistence			**X**
Bioconcentration			**X**
Cancer Health Hazard			**X**
Non-Cancer Health Hazard		**X***	
Aquatic Toxicity Hazard	**X**		
Is the chemical predicted to be a PBT by PBT Profiler?	**No**		
Overall Hazard Concern	**Human Health Hazard: Moderate** **Aquatic Hazard: High**		

* Based on systemic effects and eye irritation.

Record ID: WS-5	**CAS No.** 115-86-6
PHYSICAL/CHEMICAL PROPERTIES	
Melting Point (deg C)	50.5 (M)
Boiling Point (deg C)	245 @ 11 mm Hg (M); 389 (E)
Vapor Pressure (mm Hg)	$6.3x10^{-6}$ (M)
Water Solubility (g/L)	$1.9x10^{-3}$ (M)
Log K_{ow}	4.59 (M)
ENVIRONMENTAL TRANSPORT AND FATE:	
Transport	
Henry's Law Constant – HLC (atm-m^3/mole)	1.2×10^{-5} (M)
Soil Adsorption Coefficient – K_{oc}	2514-3561 (M)
Bioconcentration Factor – BCF	132-264 (Rainbow Trout); 218-1743 (Fathead Minnow) (M)
Persistence	
Experimental Biodeg Tests	93.8% removal as DOC in OECD 303A over 20 days; 50-100% removal within 8 days in river die-away; 83-84% over 28 days using MITI II; 10.3% removal in 40 days under anaerobic conditions in river sediment
Ultimate Biodeg Model	Weeks-months (E)
Primary Biodeg Model	Days (E)
BOD or COD	
Atmospheric Half-life	12 hours for gas phase reaction (E); Extremely low percentage of compound is in the gas phase (P)
Hydrolysis Half-life	Half-life at 20 °C: 366 days at pH 3; 406 days at pH 7, <5 days at pH 9 (M)
Volatilization Half-life for Model River	13 days (E)
Volatilization Half-life for Model Lake	152 days (E)
Removal in Sewage Treatment Plant	61% (E)
Ready Biodegradability	Ready biodegradable (M)
Byproducts	

Record ID: WS-5	**CAS No.** 115-86-6
Degradation Products	Diphenyl phosphate, phenol (M)
Metabolites	
ECOTOXICITY:	
ECOSAR Class	Esters-phosphate
Comments	*** = based on geometric mean of experimental values**
Acute Toxicity	
Fish LC_{50}	96-h LC50, 0.870 mg/L (M)
Daphnid LC_{50}	48-h LC50, 1.1 mg/L* (M)
Green Algae EC_{50}	96-h EC50, 2.0 mg/L (M)
Chronic Toxicity	
Fish ChV	0.09 (Acute/chronic ratio=10, E)
Daphnid ChV	0.1 mg/L (Acute/chronic ratio=10, E)
Green Algae ChV	≥0.140 mg/L (E) < 0.600 mg/L (M) 0.5 mg/L (Acute/chronic ratio=4, E)
Overall Hazard Concern for Aquatic Toxicity	HIGH
HEALTH EFFECTS:	
Absorption	Poor through skin as neat solid, moderate through skin in solution; moderate through lungs and GI tract based on closely related analogs (P)
CANCER HEALTH EFFECTS:	
Experimental data	
OncoLogic Results	Marginal (E)
Overall Hazard Concern for Carcinogenicity	LOW
NON-CANCER HEALTH EFFECTS:	
Acute Toxicity	Low; Rat, mouse, rabbit, oral, LD50 > 5000 mg/kg (M); rabbit, dermal, LD50 > 7900 mg/kg (M)
Eye Irritation	Moderate; Mild eye irritation, rabbits (M)

Record ID: WS-5	**CAS No.** 115-86-6
Skin Irritation	Low; Negative, rabbits (M)
Skin Sensitizer	Low; very low incidence in humans (M)
Reproductive Effects	Low; Negative in 91-112-d reproductive (incomplete)/developmental study, rats, diet, NOAEL = 690 mg/kg/day (1%) (M)
Developmental Effects	Low; Negative in 91-112-d reproductive-developmental study, rats, diet, fetal and maternal NOAELs = 690 mg/kg/day (1%)(M)
Immune System Effects	Low; 120-d repeated-dose study, rats, diet, no immune system effects, NOAEL = 700 mg/kg/day (1%) (M)
Neurotoxicity	Low; Negative in delayed neurotoxicity studies in hen at ≤10,000 mg/kg/day (oral, 6 dosing days) and cat at 700 mg/kg (subcutaneous, single dose) (M); Negative in 120-d repeated-dose neurotoxicity screening study, rats, diet, NOAEL = 711 mg/kg/day (1.0%) (M)
Genotoxicity/Mutagenicity	Low; Negative with and without metabolic activation in Ames assay, in forward mutation assay (mouse lymphoma cells *in vitro*), and in mitotic gene conversion assay (*Saccharomyces cerevisiae*) (M)
Systemic Effects	Moderate; 35-d repeated-dose study (inadequate), rats, diet, increased relative liver weight at 0.5%, NOAEL = 0.1%; 120-d repeated-dose (neurotoxicity screening) study, rats, diet, decreased body weight gain without decreased food consumption, NOAEL = 161 mg/kg/day (0.25%), LOAEL = 345 mg/kg/day (1%); 21-d repeated-dose study (inadequate), rabbits, dermal, systemic effects (M)
Overall Hazard Concern for Non-Cancer Health Effects	MODERATE

4.0 Chemical Hazard Reviews

This section contains detailed hazard reviews of available information for each of the chemicals evaluated. These detailed hazard reviews are the basis for the summary assessments in section 3.0. The summary assessments were in turn used as the basis for summary Table 2-1, which provides top-level information on all of the alternatives.

Flame Retardant Alternative WS-1:
Phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester
[Synonym: Bisphenol A bis(diphenyl phosphate)]
5945-33-5

Hazard Review

Phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester:
Existing Data Summary Table – Human Health Endpoints

T= Endpoint characterized by existing data * = Data available but not adequate	Ψ = Endpoint not applicable

Acute Toxicity	
Oral	
Dermal	
Inhalation	
Eye irritation	
Dermal irritation	
Skin sensitization	
Subchronic Toxicity	
28-Day oral	
90-Day oral	
Combined repeated dose with reproduction/ developmental toxicity screen	
21/28-Day dermal	
90-Day dermal	
28-Day inhalation	
90-Day inhalation	
Reproductive Toxicity	
Reproduction/ developmental toxicity screen	
Combined repeated dose with reproduction/ developmental toxicity screen	
Reproduction and fertility effects	

Developmental Toxicity	
Reproduction/ developmental toxicity screen	
Combined repeated dose with reproduction/ developmental toxicity screen	
Prenatal developmental	
Chronic Toxicity	
Chronic toxicity (two species)	
Combined chronic toxicity/ carcinogenicity	
Carcinogenicity	
Carcinogenicity (rat and mouse)	
Combined chronic toxicity/ carcinogenicity	

Neurotoxicity	
Acute and 28-day delayed neurotoxicity of organophosphorus substances (hen)	
Neurotoxicity screening battery (adult)	
Developmental neurotoxicity	
Additional neurotoxicity studies	
Immunotoxicity	
Immunotoxicity	
Genotoxicity	
Gene mutation in vitro	
Gene mutation in vivo	
Chromosomal aberrations in vitro	
Chromosomal aberrations in vivo	
DNA damage and repair	
Other	

Phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester:
Existing Data Summary Table – Properties, Fate, and Ecotoxicity

T= Endpoint characterized by existing data * = Data available but not adequate	Ψ = Endpoint not applicable

P/Chem Properties	
Water solubility	
Octanol/water partition coefficient	
Oxidation/reduction	
Melting point	
Boiling point	
Vapor pressure	
Odor	
Oxidation/reduction chemical incompatibility	
Flammability	
Explodability	
Corrosion characteristics	
pH	
UV/visible absorption	
Viscosity	
Density/relative density/bulk density	
Dissociation constant in water	
Henry's Law constant	

Environmental Fate	
Bioconcentration	
Fish	
Daphnids	
Green algae	
Oysters	
Earthworms	
Metabolism in fish	
Degradation and Transport	
Photolysis, atmosphere	
Photolysis, water	
Photolysis in soil	
Aerobic biodegradation	
Anaerobic biodegradation	
Porous pot test	
Pyrolysis	
Hydrolysis as a function of pH	
Sediment/water biodegradation	
Soil biodegradation w/ product identification	
Indirect photolysis in water	
Sediment/soil adsorption/desorption	

Ecotoxicity	
Aquatic Toxicity	
Fish acute LC50	
Daphnia acute EC50	
Mysid shrimp acute LC50	
Green algae EC50, NOAEC, LOAEC	
Fish chronic NOAEL, LOAEC	
Daphnia chronic NOAEC, LOAEC	
Mysid shrimp chronic NOAEC, LOAEC	
Sediment organisms	
Terrestrial Organism Toxicity	
Bird LD50 (two species)	
Bird LC50 (two species)	
Bird reproduction	
Earthworm subchronic EC50, LC50, NOAEC, LOAEC	

Chemical Identity

Phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester

Synonym	Bisphenol A bis(diphenyl phosphate) [BDP]
CAS	5945-33-5
MF	$C_{39}H_{34}O_8P_2$
MW	692.65
SMILES	c1ccccc1OP(Oc2ccccc2)(=O)Oc3ccc(cc3)C(C)(C)c4ccc(cc4)OP(=O)(Oc5ccccc5)(Oc6ccccc6)

Human Health Endpoints

The OPPTS Harmonized Test Guidelines are the preferred criteria for study adequacy, but the corresponding OECD Guidelines are also considered. The available studies generally conformed to these guidelines as well as Good Laboratory Practice guidelines. Studies that were published in a foreign language, or that were not readily available, and that were not critical to the hazard assessment were not retrieved.

The relevance of health effects studies in laboratory animals to humans needs to be considered in the context of anticipated human exposure patterns. For example, adverse effect levels measured following bolus exposure in oral gavage studies in animals may not directly pertain to human exposures from drinking water in which intakes occur over a longer time period during a day. The more gradual intakes are less likely to overwhelm detoxification processes than bolus delivery.

No published studies were located on the effect of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP; CAS No. 5945-33-5) on human health endpoints, but some data were located for mixtures (DVP 506; CN-1985; Fyrolflex-BDP) characterized as phosphoric trichloride, reaction products with bisphenol A and phenol (CAS No. 181028-79-5) and containing BDP as a major component. Data available for the mixture NcendX P-30 did not identify or specify the relative composition of the major components (Australia DHA, 2005). No quantitative compositional information was provided for most of the mixtures used in testing human health endpoints, but data were provided for one batch (No. 676/79) of DVP 506 technical (FMC AGP, 1997). This analysis reported a composition of 84.6% BDP and 10.9% phosphoric acid, bis-4-[1-4[(diphenoxyphosphinyl)oxy]phenyl]-1-methyl-ethyl]phenyl] phenyl ester (CAS No.83029-72-5). Based on this analysis, DVP 506 batch 676/79 is judged to be an adequate test material for the toxicity of BDP (tests conducted in 1997), but this judgement does not apply to tests of DVP 506 for which the batch was not specified.

An assessment of Fyrolflex-BDP referred to this material as phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (CAS No. 5945-33-5), although the description was consistent with the mixture phosphoric trichloride, reaction products with bisphenol A and phenol (CAS No. 181028-79-5) (Australia DHA, 2000). The purity of this material was stated to be 75-95%, typically containing 85% phosphoric acid, (1-

methylethylidene)di-4,1-phenylene tetraphenyl ester, 2.2-12.3% oligomers, 2.2-2.4% triphenyl phosphate, 0.07% phenol and <0.01 bisphenol A. In the absence of compositional data for the tested substance, tests conducted on this material (BPA-BDPP) provide suggestive, but not definitive evidence for the toxicological properties of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (CAS No. 5945-33-5).

ACUTE TOXICITY

Acute Oral Toxicity (OPPTS Harmonized Guideline 870.1100; OECD Guidelines 425, 420, 423, 401).

Conclusion:

The existing acute oral toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available acute oral toxicity data were guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP) as a major component. Neither NcendX P-30 nor BPA-BDPP caused death or any other sign of toxicity in male and female rats dosed by oral gavage with 2000 mg/kg (Inveresk, 1999a; Safepharm, 1997a), and similar results were obtained from dosing male and female rats with 5000 mg/kg DVP 506 or CN-1985 (FMC, 1997a; WIL Res. Labs., 1996a). No significant adverse clinical signs of toxicity or necropsy findings were observed in these studies. These results suggest that the acute oral lethality of BDP may be low.

Acute Dermal Toxicity (OPPTS Harmonized Guideline 870.1200; OECD Guideline 402)

Conclusion:

The existing acute dermal toxicity data were judged inadequate to meet the endpoint.

***Basis for Conclusion*:**

The only available acute dermal toxicity data were guideline studies on commercial mixtures (DVP 506, CN-1985; BPA:BDPP; NcendX P-30) containing unreported amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP) as a major component. None of the mixtures caused mortality in male or female rats exposed for 24 hours dermally at 2000 mg/kg (FMC, 1997b; WIL Res. Labs., 1996b; Inveresk, 1999b; SafePharm, 1997b). No necropsy or clinical signs were observed except for red nasal discharge in rats exposed to NcendX P-30). No dermal irritation was observed following treatment with DVP 506, but erythema of the application site was observed on day 1 in a majority of rats (4/5 males and 3/5

females) and desquamation in 1/5 males and 2/5 females exposed to CN-1985; erythema and desquamation completely subsided by day 9. These results suggest that the acute dermal lethality of BDP may be low.

Acute Inhalation Toxicity (OPPTS Harmonized Guideline 870.1300 (OECD Guideline 403)

Conclusion:

The existing data were judged inadequate to meet the endpoint..

Basis for Conclusion:

No studies of this type were located for phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP) or mixtures containing BDP.

Acute Eye Irritation (OPPTS Harmonized Guideline 870.2400; OECD Guideline 405)

Conclusion:

The existing eye irritation data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available acute eye irritation data were guideline studies on commercial mixtures (CN-1985; DVP 506; BPA:BDPP; NcendX P-30) containing unreported amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP) as a major component. Tests in rabbits receiving 0.1 mL of undiluted mixture indicated minimal irritation to the eyes. One hour after application of DVP 506, severe discharge was observed that resolved within 72 hours (FMC, 1997c). Primary eye irritation indices in this study were 6.0, 3.7, 2.0 and 0 at 1, 24 48, and 72 hours, respectively. Application of CN-1985 resulted in a maximum average score of 2.0 after 1 hour associated with minor conjunctival irritation in all animals that resolved on or before day 7 (WIL Res. Labs., 1996c). BPA:BDPP and NcendX P-30 elicited minimal conjunctival redness one hour after treatment that resolved within 24 hours, and the latter also caused lacrimation that resolved within 3-5 days (Inveresk, 1999c; Safepharm, 1997c). No effects were observed in the cornea or iris in any of these studies. These results suggest that BDP may be minimally irritating to the eyes.

Acute Dermal Irritation (OPPTS Harmonized Guideline 870.2500; OECD Guideline 404)

Conclusions:

The existing acute dermal irritation data were judged inadequate to meet the endpoint.

Basis for Conclusions:

The only available acute dermal irritation data were guideline studies on commercial mixtures (CN-1985; DVP 506; BPA:BDPP; NcendX P-30) containing unreported amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP) as a major component. No erythema or edema was observed on rabbit skin at any time during the three days following a 4-hour application of 0.5 mL DVP 506 or BPA:BDPP under occlusive covering (FMC, 1997d; Safepharm, 1997d). The primary irritation index in these studies was 0/8.0, indicating these mixtures were non-irritating to the skin. Slight irritation was observed in the skin of rabbits dermally exposed to 0.5 mL of CN-1985 (primary irritation index 0.3) or NcendX P-30 for 4-hours under a semi-occlusive covering (Inveresk, 1999d; WIL Res Labs., 1996d). For both mixtures, a majority of animals exhibited erythema during the first three days that was completely resolved by day 7. The results suggest that the potential for BDP to cause acute dermal irritation may be low.

Skin Sensitization (OPPTS Harmonized Guideline 870.2600; OECD Guideline 429)

Conclusion:

The existing skin sensitization data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available skin sensitization data were from guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP) as a major component. Negative results were reported for DVP 506 in the Buehler test in guinea pigs (FMC, 19973) and for CN-1985, NcendX P-30 and BPA:BDPP in the guinea pig maximization test (Inveresk, 1999e; Safepharm, 1997e; WIL Res. Labs., 1998a). The results suggest that the potential for BDP to induce skin sensitization may be low.

SUBCHRONIC TOXICITY

Subchronic Oral Toxicity (28-day, 90-day, or combined with reproductive/developmental)

Conclusion:

The existing subchronic oral toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available subchronic oral toxicity data were from guideline 28-day studies on commercial mixtures containing unreported amounts of phosphoric acid, (1-methylethylidene)di-

4,1-phenylene tetraphenyl ester (BDP) as a major component. These studies reported NOAEL values in the range of 1000-1968 mg/kg/day (FMC, 1997f; Safepharm, 1997f; Springborn, 2000; WIL Res. Labs., 1998b). Results for the mixtures indicate the possibility that the subchronic oral toxicity of pure BDP may be low.

- **Repeated Dose 28-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3050; OECD Guideline 407)**

No adverse effects were observed in four 28-day assays on mixtures containing BDP. NOAELs of 1000 mg/kg/day were reported for rats exposed by oral gavage to CN-1985 in corn oil, NcendX P-30 in polyethylene glycol 400, or BPA:BDPP (vehicle not reported) (Safepharm, 1997f; Springborn, 2000; WIL Res. Labs., 1998b). No adverse effects were observed in male or female rats exposed to DVP 506 in the diet at concentrations as high as 20,000 ppm (FMC, 1997f). In this study the NOAELs were 1862 mg/kg/day for males and 1968 mg/kg/day for females.

- **90-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3100; OECD Guideline 408)**

No studies of this type were located.

- **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**

No studies of this type were located.

Subchronic Dermal Toxicity (21/28-day or 90-day)

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No study was located that followed or was similar to the two guidelines listed below or otherwise addressed the subchronic dermal toxicity of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP).

- **21/28-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3200 (OECD Guideline 410)**

- **90-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3250; OECD Guideline 411)**

Subchronic Inhalation Toxicity (90-day Inhalation Toxicity (OPPTS Harmonized Guideline 870.3250 (OECD Guideline 411)

Conclusion:

The existing data were judged inadequate to meet the endpoint

Basis for Conclusion:

No study was located that followed or was similar to the guideline or otherwise addressed the subchronic inhalation toxicity of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP)

REPRODUCTIVE TOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No study was located that followed or was similar to the three guidelines listed below or otherwise addressed the reproductive toxicity of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP)

- **Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)**
- **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**
- **Reproduction and Fertility Effects (OPPTS Harmonized Guideline 870.3800; OECD Guideline 416)**

DEVELOPMENTAL TOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint

Basis for Conclusion:

The only available developmental toxicity data were from a guideline study on a commercial mixture containing unreported amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP) as a major component. NOAELs of 1000 mg/kg/day were reported in a prenatal developmental toxicity study in rats exposed by oral gavage to CN-1985 (WIL Res. Labs., 1998c, 1998d). The results suggest the possibility that the developmental toxicity of BDP may be low.

- **Prenatal Developmental Toxicity Study (OPPTS Harmonized Guideline 870.3700; OECD Guideline 414)**

In range-finding and main guideline studies, no adverse treatment-related maternal or developmental effects were observed in rats exposed by oral gavage in corn oil to CN-1985 at doses as high as 1000 mg/kg/day on gestational days 6-19 (WIL Res. Labs., 1998c, 1998d). There were no treatment-related effects on maternal food consumption, body weight, uterine parameters, or the incidences of fetal malformations or variations. Clinical signs observed in dams during dosing were related to aversion of the taste of the test material.

- **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**

No studies of this type were located.

- **Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)**

No studies of this type were located.

CHRONIC TOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No study was located that followed or was similar to the two guidelines listed below or otherwise addressed the chronic toxicity of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP)

- **Chronic Toxicity (OPPTS Harmonized Guideline 870.4100; OECD Guideline 452)**
- **Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)**

CARCINOGENICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No study was located that followed or was similar to the two guidelines listed below or otherwise addressed the carcinogencity of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP).

- **Carcinogenicity (OPPTS Harmonized Guideline 870.4200; OECD Guideline 451)**
- **Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)**

NEUROTOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No neurotoxicity studies conforming to any of the following or similar guidelines were available for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP) or defined mixtures containing BDP. In a 28-day oral (gavage) toxicity study, no adverse effects were noted in weekly neurotoxicological examinations of rats exposed to ≤1000 mg/kg/day NcendX P-30, an undefined mixture containing BDP as a major component (Australia DHA, 2005; Springborn, 2000). These results suggest that the potential for BDP to cause neurotoxicity may be low.

- **Acute and 28-Day Delayed Neurotoxicity of Organophosphorus Substances (OPPTS Harmonized Guideline 870.6100; OECD Guideline 418, 419)**
- **Neurotoxicity (Adult)**: **Neurotoxicity Screening Battery (OPPTS Harmonized Guideline 870.6200; OECD Guideline 424)**
- **Developmental Neurotoxicity: Developmental Neurotoxicity Study (OPPTS Harmonized Guideline 870.6300)**

Additional neurotoxicity studies:

- Schedule-Controlled Operant Behavior (mouse or rat) (OPPTS Harmonized Guideline 870.6500)
- Peripheral Nerve Function (rodent) (OPPTS Harmonized Guideline 870.6850)
- Sensory Evoked Potentials (rat, pigmented strain preferred) (OPPTS Harmonized Guideline 870.6855)

These studies may be indicated, for example, to follow up neurotoxic signs seen in other studies, or because of structural similarity of the substance to neurotoxicants that affect these endpoints. These studies may be combined with other toxicity studies.

Conclusion: These endpoints do not appear to be applicable to phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP).

Basis for Conclusion: Although there are no studies addressing these endpoints, there are no reliable data for BDP, and no structure-activity considerations, that currently indicate a need for these follow-up studies.

IMMUNOTOXICITY (OPPTS Harmonized Guideline 870.7800)

***Conclusion*:**

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No study was located that followed the guideline or otherwise addressed the immunotoxicity of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP).

GENOTOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

Negative studies for mutagenicity in bacteria and chromosomal aberrations in vitro were available for phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP) in a defined mixture, but not enough detail was included in the secondary source to determine whether the studies were adequate (Covance Labs., 1997a, 1997b as reported in Green Lakes,

2003a). Additional negative guideline studies for mutagenicity in bacteria, chromosomal aberration in vitro, and micronucleus formation in vivo were conducted on mixtures containing unreported amounts of BDP as a major component. These results suggest the possibility that the genotoxicity of BDP may be low.

Gene Mutation in Vitro:

- **Bacterial Reverse Mutation test (OPPTS Harmonized Guideline 870.5100; OECD Guideline 471)**

The secondary source (Green Lakes, 2003a) did not stipulate a guideline or provide sufficient detail (for example on the use of positive controls) to determine whether the negative bacterial mutagenesis assay on the defined mixture DVP 506 (batch 676/79) was reliable.

Type: Bacterial reverse mutation
Species, strain: *Salmonella typhimurium* and *Escherichia coli* (strains not reported)
Metabolic activation: Tested with and without Aroclor-induced rat liver S9
Concentrations: 0, 50, 100, 500, 1000, 5000 :g/plate.
Purity: 84.6% (DVP 506, batch 676/79)
Method: Plate incorporation assay. Results of first experiment were confirmed in a second assay. No details on time of exposure, bacterial strains, or the use of positive or negative controls were provided in the secondary source.
Results: No positive increase in revertant frequency was observed in either assay with or without metabolic activation.
Reference: Covance Labs. (1997a) as reported in Green Lakes (2003a)

Additional information.

Assays on undefined mixures also reported negative results for mutagenicity in bacteria. In guideline studies, neither BPA:BDPP (containing BDP as a major undefined component) nor NcendX P-30 (BDP composition unknown) caused an increase in the revertant frequency of *Salmonella typhimurium* strains TA1535, TA1537, TA98 or TA100 or *Escherichia coli* WP2*uvr*A at concentrations as high as 5 mg/plate (Inveresk, 1999f; Safepharm, 1997g). In a pre-incubation assay, the mixture CN-1985 (BDP content not reported) did not increase the mutation frequency in *Salmonella typhimurium* or *Escherichia coli* at concentrations as high as 5 mg/plate with or without metabolic activation with S9 from Aroclor-induced rat liver (Microbiological Associates, 1995); bacterial strains and use of positive and negative controls were not reported in the secondary source (Green Lakes, 2003a). The results of these studies suggest that the mutagenic potential of BDP to bacteria may be low.

- **In vitro Mammalian Cell Gene Mutation Test (OPPTS Harmonized Guideline 870.5300; OECD Guideline 476)**

No study of this type was located.

- **Mitotic Gene Conversion in Saccharomyces cerevisiae (OPPTS Harmonized Guideline 870.5575)**

No study of this type was located.

Gene Mutation in Vivo

No study of this type was located.

Chromosomal Aberrations in Vitro

- **In vitro Chromosome Aberration Test (OPPTS Harmonized Guideline 870.5375)**

The report of the available study on a mixture (DVP 506 676/79) containing a defined amount of BDP did not stipulate a specific guideline and was missing details (such as use of positive and negative controls) required to determine whether the negative chromosomal aberration assay in human lymphocytes was reliable.

Type: In vitro chromosome aberration assay
Species, strain: Human peripheral lymphocytes
Metabolic activation: None, S9 derived from rat liver (inducing chemical not reported)
Concentrations: 0, and 31.3 to 1500 μL/mL (the high concentration was limited by the formation of precipitate)
Purity: 84.6% (DVP 506, batch 676/79)
Method: Two independent assays were conducted with multiple harvest times with or without metabolic activation. No information on time of exposure or use of positive and negative controls was reported in the secondary source.
Results: BDP did not increase in the frequency of chromosomal aberrations in human lymphocytes with or without activation in two independent assays.
Reference: Covance Labs. (1997b) as cited in Green Lakes (2003a)

Additional information.

Guideline studies on undefined mixtures with unknown (CN-1985; NcendX P-300) or unreported amounts of BDP as a major component (BPA:BDPP) also reported negative results for chromosomal aberration in vitro with or without metabolic activation. CN-1985 tested at 10 concentrations between 6.4 and 3260 μL/mL did not increase the incidence of polyploidy or chromosomal aberrations in cultured human lymphocytes (Huntingdon, 1998). BPA:BDPP tested at six concentrations between 156.25 and 5000 μL/mL did not increase the incidence of chromosomal aberrations in Chinese hamster lung cells (Safepharm, 1997h). Negative results were also reported in Chinese hamster ovary cells cultured with NcendX P-30 at concentrations

between 20 and 5000 μL/mL (Inveresk, 2000a). The results of these studies suggest that the potential for BDP to induce chromosomal aberrations in vitro may be low.

Chromosomal Aberrations in Vivo

- **Mammalian Erythrocyte Micronucleus Test (OPPTS Harmonized Guideline 870.5395; OECD Guideline 474)**

Guideline studies on undefined mixtures containing BDP as a major component reported negative results in micronucleus tests in vivo. No increase in the frequency of bone marrow erythrocyte micronuclei was observed in male or female mice given a single intraperitoneal injection of 1250-5000 mg/kg CN-1985 (BDP content not reported) and examined after 24, 48 and 72 hours (MA BioServices, 1998). NcendX P-30 did not increase the frequency of micronucleus formation in male or female mice dosed at 2000 mg/kg by oral gavage in corn oil and examined after 48 hours (Inveresk, 2000b). The results of these studies suggest that the potential for BDP to induce micronucleus formation in vivo may be low.

DNA Damage and Repair

No study of this type was located.

Ecotoxicity

Acute Toxicity to Aquatic Organisms

Conclusion:

The currently available data are not adequate to satisfy the acute toxicity endpoints for fish, aquatic invertebrates, or algae.

Basis for Conclusion:
No pertinent acute toxicity studies with fish, aquatic invertebrates, or algae for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester were located that addressed the endpoints in the guidelines listed below.

- **Acute Toxicity to Freshwater and Marine Fish (OPPTS Harmonized Guideline 850.1075; OECD Guideline 203)**

Experimental fish LD_{50} values of >0.025 mg/L (Australia DHA, 2005), >1 mg/L (Australia DHA, 2000), >100 mg/L (Great Lakes, 2003c) and >500 mg/L (Great Lakes 2003c) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the acute toxicity values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results. In addition, the experimental LD_{50} values are all much greater than the estimated water solubility for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester, suggesting no effect at saturation.

- **Acute Toxicity to Freshwater Invertebrates (OPPTS Harmonized Guideline 850.1010; OECD Guideline 202)**

Experimental daphnia magna EC_{50} values of >0.02 mg/L (Australia DHA, 2005), >0.034 mg/L (Australia DHA, 2005), >1 mg/L (Australia DHA, 2000), and >100 mg/L (Great Lakes 2003a) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the acute toxicity values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results. In addition, the experimental EC_{50} values are all much greater than the estimated water solubility for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester, suggesting no effect at saturation.

- **Acute Toxicity to Marine/Estuarine Invertebrates (OPPTS Harmonized Guideline 850.1035)**
- **Algal Toxicity (OPPTS Harmonized Guideline 850.5400; OECD Guideline 201)**

Experimental algal EC_{50} values of >0.02 mg/L (Australia DHA, 2005), >1 mg/L (Australia DHA, 2000), and >100 mg/L (Great Lakes, 2003c) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the acute toxicity values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results. In addition, the experimental EC_{50} values are all much greater than the estimated water solubility for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester, suggesting no effect at saturation.

Chronic Toxicity to Aquatic Organisms

Conclusion:

The currently available data are not adequate to satisfy the chronic toxicity endpoints for fish or aquatic invertebrates.

Basis for Conclusion:

No pertinent chronic toxicity studies with fish or aquatic invertebrates for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester were located that addressed the endpoints in the guidelines listed below.

- **Chronic Toxicity to Freshwater and Marine Fish (OPPTS Harmonized Guideline 850.1400; OECD Guideline 210)**

Experimental fish NOEC values of 5 mg/L (Great Lakes, 2003a) and >100 mg/L (Great Lakes, 2003a) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the chronic toxicity values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results. In addition, the experimental NOEC values are all much greater than the estimated water solubility for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester, suggesting no effect at saturation.

- **Chronic Toxicity to Freshwater Invertebrates (OPPTS Harmonized Guideline 850.1300; OECD Guideline 211)**

An experimental daphnia magna NOEC value of >5 mg/L (Great Lakes, 2003a) has been reported for a commercial mixture of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contains varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of this mixture is not specified and, therefore, the chronic toxicity value for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from this results. In addition, the experimental NOEC value is much greater than the estimated water solubility for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester, suggesting no effect at saturation.

- **Chronic Toxicity to Marine/Estuarine Invertebrates (OPPTS Harmonized Guideline 850.1350)**

Acute and Subchronic Toxicity to Terrestrial Organisms

Conclusion:

The currently available data are not adequate to satisfy the acute or subchronic toxicity endpoints for terrestrial organisms.

Basis for Conclusion:

No pertinent acute oral, acute dietary, or reproductive toxicity studies with birds and no subchronic toxicity studies with earthworms for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester were located that addressed the endpoints in the guidelines listed below.

- **Acute Oral Toxicity in Birds (OPPTS Harmonized Guideline 850.2100)**
- **Acute Dietary Toxicity in Birds (OPPTS Harmonized Guideline 850.2200; OECD Guideline 205)**
- **Reproductive Toxicity in Birds (OPPTS Harmonized Guideline 850.2300; OECD Guideline 206)**
- **Earthworm Subchronic Toxicity (OPPTS Harmonized Guideline 850.6200; OECD Guideline 207)**

An experimental earthworm NOEC value of 1,000 mg/L (Great Lakes,, 2003c) has been reported for a commercial mixture of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contains varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of this mixture is not specified and, therefore, the chronic toxicity value for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from this results.

Physical/Chemical Properties

Phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester

CAS	5945-33-5
MF	$C_{39}H_{34}O_8P_2$
MW	692.65
SMILES	c1ccccc1OP(Oc2ccccc2)(=O)Oc3ccc(cc3)C(C)(C)c4ccc(cc4)OP(=O)(Oc5ccccc5)(Oc6ccccc6)

Water Solubility (mg/L):

Conclusion:

The currently available data are not adequate to satisfy the water solubility endpoint.

Basis for Conclusion:

Experimental data for the water solubility of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester has been reported to be 0.415 g/L (Australia DHA, 2000). However, the compositional analysis indicates that the substance is only 75-95% pure and contains oligomeric material. This suggests that the substance may actually be phosphoric trichloride, reaction products with bisphenol A and phenol, which has been mislabeled as phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. In the rest of this document, information contained in this source will be included with the data reported for phosphoric trichloride, reaction products with bisphenol A and phenol.

Experimental water solubility values ranging from <0.02 mg/L to 10 mg/L (Australia DOH, 2005; Chang Chun, no date; Great lakes, 2003a, 2003b, 2003c[1] have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the water solubility values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined. from these results.

Log K_{ow}:

Conclusion:

The currently available data are not adequate to satisfy the log K_{ow} endpoint.

Basis for Conclusion:

Experimental data for the log K_{ow} of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental log K_{ow} values ranging from 4.0 to >6 (Australia DHA, 2000, 2005; Great Lakes, 2003a, 2003b, 2003c; Wildlife International Ltd., 2002) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified in the experimental study details and, therefore, the log K_{ow} values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results.

Oxidation/Reduction:

Conclusion:

The currently available data are not adequate to satisfy the oxidation/reduction endpoint.

Basis for Conclusion:

No data is available for the oxidation/reduction endpoint.

Melting Point:

Conclusion:

The currently available data are not adequate to satisfy the melting point endpoint.

Basis for Conclusion:

Experimental data for the melting point of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental melting point values of 7 °C (Great Lakes 2003a) 8 °C (Akzo Noble, 1999; Great Lakes 2003b) and 41-69 °C (Australia DHA, 2000) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the melting point values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results.

Boiling Point:

Conclusion:

The currently available data are not adequate to satisfy the boiling point endpoint.

Basis for Conclusion:

Experimental data for the boiling point of pure pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental boiling point values of >220 °C (Great Lakes 2003a), >240-250 °C (Australia DHA, 2005) and >300 °C (Akzo Noble, 1999; Great Lakes 2003b, 2003c), as well as experimental decomposition temperatures of 201 °C (Australia DHA, 2000) and >350 °C (Great Lakes 2003a) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the boiling point values for pure pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results.

Vapor Pressure (torr):

Conclusion:

The currently available data are not adequate to satisfy the vapor pressure endpoint.

Basis for Conclusion:

Experimental data for the vapor pressure of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental vapor pressure values ranging from $2.3x10^{-18}$ torr to 0.18 torr (Akzo Noble, 1999; Australia DHA, 2005; Chang Chun, no date; Great Lakes 2003a, 2003b, 2003c) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the vapor pressure values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results.

Odor:

Conclusion:

The currently available data are not adequate to satisfy the odor endpoint.

Basis for Conclusion:

No data is available for the odor endpoint.

Oxidation/Reduction Chemical Incompatibility:

Conclusion:

The currently available data are not adequate to satisfy the oxidation/reduction chemical incompatibility endpoint.

Basis for Conclusion:

No data is available for the oxidation/reduction chemical incompatibility endpoint.

Flammability:

Conclusion:

The currently available data are not adequate to satisfy the flammability endpoint.

Basis for Conclusion:

Experimental data for the flammability of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental flammability values of >400 °C (Australia DHA, 2000; Great Lakes 2003a) and 625 °C (Australia DHA, 2005) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the flammability values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results.

Flash Point:

Conclusion:

The currently available data are not adequate to satisfy the flash point endpoint.

Basis for Conclusion:

Experimental data for the flash point of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental flash point values of >200 °C (Great Lakes, 2003a), >250 °C (Great Lakes, 2003c), 281 °C (Great Lakes, 2003a), >300 °C (Australia DHA, 2000), >334 °C (Chang

Chun, no date) and >360 °C (Australia DHA, 2005) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the flash point values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results.

Explodability:

Conclusion:

The currently available data are not adequate to satisfy the explodability endpoint.

Basis for Conclusion:

No data is available for the explodability endpoint.

Corrosion Characteristics:

Conclusion:

The currently available data are not adequate to satisfy the corrosion characteristics endpoint.

Basis for Conclusion:

No data are available for the corrosion characteristics endpoint.

pH:

Conclusion:

The currently available data are not adequate to satisfy the pH endpoint.

Basis for Conclusion:

No data are available for the pH endpoint.

UV/VIS Absorption:

Conclusion:

The currently available data are not adequate to satisfy the UV/Vis absorption endpoint.

Basis for Conclusion:

No data are available for the UV/Vis absorption endpoint.

Viscosity:

Conclusion:

The currently available data are not adequate to satisfy the viscosity endpoint.

Basis for Conclusion:
Experimental data for the viscosity of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental viscosity values of 100 cSt (Great Lakes, 2003c) and 5040 cps (Great Lakes, no date) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the viscosity values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results.

Density/Relative Density/Bulk Density:

Conclusion:

The currently available data are not adequate to satisfy the density endpoint.

Basis for Conclusion:

Experimental data for the density of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental density values ranging from 1.2576 g/cc to 1.26 g/cc (Australia DHA, 2005; Chang Chun, no date; Great Lakes, no date,2003a, 2003c) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the density values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results.

Dissociation Constant in Water:

Conclusion:

The currently available data are not adequate to satisfy the dissociation constant in water endpoint.

Basis for Conclusion:

No data are available for the dissociation constant in water endpoint.

Henry's Law Constant:

Conclusion:

The currently available data are not adequate to satisfy the Henry's law constant endpoint.

Basis for Conclusion:

No data are available for the Henry's law constant endpoint.

Environmental Fate

Bioconcentration

Fish:

Conclusion:

The currently available data are not adequate to satisfy the fish bioconcentration endpoint.

Basis for Conclusion:

No data are available for the fish bioconcentration endpoint.

Daphnids:

Conclusion:

The currently available data are not adequate to satisfy the daphnid bioconcentration endpoint.

Basis for Conclusion:

No data are available for the daphnid bioconcentration endpoint.

Green Algae:

Conclusion:

The currently available data are not adequate to satisfy the green algae bioconcentration endpoint.

Basis for Conclusion:

No data are available for the green algae bioconcentration endpoint.

Oysters:

Conclusion:

The currently available data are not adequate to satisfy the oysters bioconcentration endpoint.

Basis for Conclusion:

No data are available for the oysters bioconcentration endpoint.

Earthworms:

Conclusion:

The currently available data are not adequate to satisfy the earthworm bioconcentration endpoint.

Basis for Conclusion:
No data are available for the earthworm bioconcentration endpoint.

Fish Metabolism:

Conclusion:

The currently available data are not adequate to satisfy the fish metabolism endpoint.

Basis for Conclusion:
No data are available for the fish metabolism endpoint.

Degradation

Photolysis in the Atmosphere:

Conclusion:

The currently available data are not adequate to satisfy the photolysis in the atmosphere endpoint.

Basis for Conclusion:

No data are available for the photolysis in the atmosphere endpoint.

Photolysis in Water:

Conclusion:

The currently available data are not adequate to satisfy the photolysis in water endpoint.

Basis for Conclusion:

No data are available for the photolysis in water endpoint.

Photolysis in Soil:

Conclusion:
The currently available data are not adequate to satisfy the photolysis in soil endpoint.

Basis for Conclusion:

No data are available for the photolysis in soil endpoint.

Aerobic Biodegradation:

Conclusion:
The currently available data are not adequate to satisfy the aerobic biodegradation endpoint.

Basis for Conclusion:

Experimental data for the aerobic biodegradation of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental aerobic biodegradation values of 21.5% and 15.84% in 29 days in activated sludge (Great Lakes, 2003a), and 2% in 28 days in sewage sludge (Australia DHA, 2005), and 3-6% in 28 days in sewage sludge (Australia DHA, 2000) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the aerobic biodegradation values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results.

Anaerobic Biodegradation:

Conclusion:

The currently available data are not adequate to satisfy the anaerobic biodegradation endpoint.

Basis for Conclusion:

No data are available for the anaerobic biodegradation endpoint.

Porous Pot Test:

Conclusion:

The currently available data are not adequate to satisfy the porous pot test endpoint.

Basis for Conclusion:

No data are available for the porous pot test endpoint.

Pyrolysis:

Conclusion:

The currently available data are not adequate to satisfy the pyrolysis endpoint.

Basis for Conclusion:
No data are available for the pyrolysis endpoint.

Hydrolysis as a Function of pH:

Conclusion:

The currently available data are not adequate to satisfy the hydrolysis as a function of pH endpoint.

Basis for Conclusion:

Experimental data for the hydrolysis as a function of pH of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental hydrolysis half-life values of >1 year at pHs 4, 7 and 9 (Australia DHA, 2000) and of between 1 day and 1 year at pHs 4, 7 and 9 (Great Lakes 2003a) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the hydrolysis values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results.

Sediment/Water Biodegradation:

Conclusion:

The currently available data are not adequate to satisfy the sediment/water biodegradation endpoint.

Basis for Conclusion:

Experimental data for the sediment/water biodegradation of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental sediment/water biodegradation DT(50) values of 762 days for sandy loam and 537 days (Great Lakes, 2003a) for sandy silt loam have been reported for

commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the sediment/water biodegradation values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results.

Soil Biodegradation with Product Identification:

Conclusion:

The currently available data are not adequate to satisfy the soil biodegradation endpoint.

Basis for Conclusion:

Experimental data for the soil biodegradation of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental soil biodegradation studies showing no significant degradation after 120 days (Great Lakes, 2003a) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the soil biodegradation values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results.

Indirect Photolysis in Water:

Conclusion:

The currently available data are not adequate to satisfy the indirect photolysis in water endpoint.

Basis for Conclusion:

No data are available for the indirect photolysis in water endpoint.

Sediment/Soil Adsorption/Desorption:

Conclusion:

The currently available data are not adequate to satisfy the sediment/soil adsorption/desorption endpoint.

Basis for Conclusion:

Experimental data for the sediment/soil adsorption/desorption of pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental sediment/soil adsorption/desorption log K_{oc} values of > 4.53 (Australia DHA, 2000), >5.4 (Great Lakes, 2003a) and 6.0-18.0 (Australia DHA, 2005) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the sediment/soil adsorption/desorption values for pure phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester cannot be determined from these results.

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Flame Retardant Alternative WS-2:
Phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester
83029-72-5

Hazard Review

Phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester: Existing Data Summary Table – Human Health Endpoints

T= Endpoint characterized by existing data * = Data available but not adequate	Ψ = Endpoint not applicable

Acute Toxicity	
Oral	
Dermal	
Inhalation	
Eye irritation	
Dermal irritation	
Skin sensitization	
Subchronic Toxicity	
28-Day oral	
90-Day oral	
Combined repeated dose with reproduction/ developmental toxicity screen	
21/28-Day dermal	
90-Day dermal	
28-Day inhalation	
90-Day inhalation	
Reproductive Toxicity	
Reproduction/ developmental toxicity screen	
Combined repeated dose with reproduction/ developmental toxicity screen	
Reproduction and fertility effects	

Developmental Toxicity	
Reproduction/ developmental toxicity screen	
Combined repeated dose with reproduction/ developmental toxicity screen	
Prenatal developmental	
Chronic Toxicity	
Chronic toxicity (two species)	
Combined chronic toxicity/ carcinogenicity	
Carcinogenicity	
Carcinogenicity (rat and mouse)	
Combined chronic toxicity/ carcinogenicity	

Neurotoxicity	
Acute and 28-day delayed neurotoxicity of organophosphorus substances (hen)	
Neurotoxicity screening battery (adult)	
Developmental neurotoxicity	
Additional neurotoxicity studies	
Immunotoxicity	
Immunotoxicity	
Genotoxicity	
Gene mutation in vitro	
Gene mutation in vivo	
Chromosomal aberrations in vitro	
Chromosomal aberrations in vivo	
DNA damage and repair	
Other	

Phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester: Existing Data Summary Table – Properties, Fate, and Ecotoxicity

T= Endpoint characterized by existing data * = Data available but not adequate	Ψ = Endpoint not applicable

P/Chem Properties	
Water solubility	
Octanol/water partition coefficient	
Oxidation/reduction	
Melting point	
Boiling point	
Vapor pressure	
Odor	
Oxidation/reduction chemical incompatibility	
Flammability	
Explodability	
Corrosion characteristics	
pH	
UV/visible absorption	
Viscosity	
Density/relative density/bulk density	
Dissociation constant in water	
Henry's Law constant	

Environmental Fate	
Bioconcentration	
Fish	
Daphnids	
Green algae	
Oysters	
Earthworms	
Metabolism in fish	
Degradation and Transport	
Photolysis, atmosphere	
Photolysis, water	
Photolysis in soil	
Aerobic biodegradation	
Anaerobic biodegradation	
Porous pot test	
Pyrolysis	
Hydrolysis as a function of pH	
Sediment/water biodegradation	
Soil biodegradation w/ product identification	
Indirect photolysis in water	
Sediment/soil adsorption/desorption	

Ecotoxicity	
Aquatic Toxicity	
Fish acute LC50	
Daphnia acute EC50	
Mysid shrimp acute LC50	
Green algae EC50, NOAEC, LOAEC	
Fish chronic NOAEL, LOAEC	
Daphnia chronic NOAEC, LOAEC	
Mysid shrimp chronic NOAEC, LOAEC	
Sediment organisms	
Terrestrial Organism Toxicity	
Bird LD50 (two species)	
Bird LC50 (two species)	
Bird reproduction	
Earthworm subchronic EC50, LC50, NOAEC, LOAEC	

Chemical Identity

Phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester

CAS	83029-72-5
MF	$C_{60}H_{53}O_{12}P_3$
MW	1059.00
SMILES	c1ccccc1OP(Oc2ccccc2)(=O)Oc3ccc(cc3)C(C)(C)c4ccc(cc4)OP(=O)(Oc5ccccc5)Oc6ccc(cc6)C(C)(C)c7ccc(cc7)OP(=O)(Oc8ccccc8)Oc9ccccc9

Human Health Endpoints

The OPPTS Harmonized Test Guidelines are the preferred criteria for study adequacy, but the corresponding OECD Guidelines are also considered. The available studies generally conformed to these guidelines as well as Good Laboratory Practice guidelines. Studies that were published in a foreign language, or that were not readily available, and that were not critical to the hazard assessment were not retrieved.

The relevance of health effects studies in laboratory animals to humans needs to be considered in the context of anticipated human exposure patterns. For example, adverse effect levels measured following bolus exposure in oral gavage studies in animals may not directly pertain to human exposures from drinking water in which intakes occur over a longer time period during a day. The more gradual intakes are less likely to overwhelm detoxification processes than bolus delivery.

No studies were located on the effect of pure phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester (CAS No. 83029-72-5) on human health endpoints. Some data were located for mixtures (DVP 506; CN-1985; NcendX P-30; Fyrolflex-BDP) characterized as phosphoric trichloride, reaction products with bisphenol A and phenol (CAS No. 181028-79-5) and containing unknown amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester (Great Lakes, 2003a; Australia DHA, 2000, 2005). Compositional analysis of DVP 506 batch 676/79 revealed only 10.9% of this compound, with the major component being 84.6% phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP) (FMC APG, 1997). Similarly, Fyrolflex-BDP was reported to contain typically 85% phosphoric acid, (1-methylethylidene)di-4,1-phenylene tetraphenyl ester (BDP) and only 2.2-12.3% oligomers, of which would include phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester (Australia DHA, 2000). Thus none of the data on the mixtures provide any useful information as to the potential toxicity of the minor component to human health endpoints.

ACUTE TOXICITY

Acute Oral Toxicity (OPPTS Harmonized Guideline 870.1100; OECD Guidelines 425, 420, 423, 401).

Conclusion:

The existing acute oral toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only acute oral toxicity data were guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester as a minor component. Neither NcendX P-30 nor BPA-BDPP caused death or any other sign of toxicity in male and female rats dosed by oral gavage at 2000 mg/kg (Inveresk, 1999a; Safepharm, 1997a), and similar results were observed in rats dosed with 5000 mg/kg DVP 506 or CN-1985 (FMC, 1997a; WIL Res. Labs., 1996a). No significant adverse clinical signs of toxicity or necropsy findings were observed in these studies The acute oral lethality of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these studies.

Acute Dermal Toxicity (OPPTS Harmonized Guideline 870.1200; OECD Guideline 402)

Conclusion:

The existing acute dermal toxicity data were judged inadequate to meet the endpoint.

***Basis for Conclusion*:**

The only acute dermal toxicity data were guideline studies on commercial mixtures (CN-1985; DVP 506; BPA:BDPP; NcendX P-30) containing unreported amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester as a minor component None of the mixtures caused mortality in male or female rats exposed for 24 hours dermally at 2000 mg/kg (FMC, 1997b; Inveresk, 1999b; Safepharm, 1997b; WIL Res. Labs., 1996b). No necropsy findings or significant clinical signs were observed except for red nasal discharge in rats exposed to NcendX P-30. The acute dermal lethality of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these studies.

Acute Inhalation Toxicity (OPPTS Harmonized Guideline 870.1300 (OECD Guideline 403)

Conclusion:

The existing data were judged inadequate to meet the endpoint..

Basis for Conclusion:

No studies of this type were located for pure phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester or defined mixtures where this compound was a major component.

Acute Eye Irritation (OPPTS Harmonized Guideline 870.2400; OECD Guideline 405)

Conclusion:

The existing eye irritation data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only acute eye irritation data were from guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester as a minor component. Minimal irritation was observed following application of 0.1 mL of DVP 506 or CN-1985 to the eyes of rabbits, elicited lacrimation in 3/3 animals on the first day (FMC, 1997c; WIL Res. Labs., 1996c). In similar studies, NcendX P-30 and BPA:BDPP caused minimal conjunctival redness one hour after treatment, and the former elicited discharge for 3-5 days (Inveresk, 1999c; Safepharm, 1997c). No effects on the iris or cornea were observed with any mixture. The potential for phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester to cause eye irritation cannot be determined from this study.

Acute Dermal Irritation (OPPTS Harmonized Guideline 870.2500; OECD Guideline 404)

Conclusions:

The existing dermal irritation data were judged inadequate to meet the endpoint.

Basis for Conclusions:

The only acute dermal irritation data were from guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester as a minor component. In tests on rabbit skin, DVP 506 and BPA:BDPP were non-irritating, whereas CN-1985 and NcendX P-30 were slightly irritating (FMC, 1997d; Inveresk, 1999d; Safepharm, 1997d; WIL Res Labs., 1996d). The potential of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester to cause skin irritation cannot be determined from these studies.

Skin Sensitization (OPPTS Harmonized Guideline 870.2600; OECD Guideline 429)

Conclusion:

The existing skin sensitization data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only acute skin sensitization data were from guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester as a minor component. Negative results were reported for DVP 506 in the Buehler test in guinea pigs (FMC, 1997e) and for CN-1985, NcendX P-30 and BPA:BDPP in the guinea pig maximization test (Inveresk, 1999e; Safepharm, 1997e; WIL Res. Labs., 1998a). The skin sensitization properties of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester ester cannot be determined from this study.

SUBCHRONIC TOXICITY

Subchronic Oral Toxicity (28-day, 90-day, or combined with reproductive/developmental)

Conclusion:

The existing subchronic oral toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available subchronic oral toxicity data were from four guideline 28-day studies on commercial mixtures containing unreported amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester as a minor component. These studies reported NOAEL values in the range of 1000-1968 mg/kg/day (FMC, 1997f; WIL Res. Labs., 1998b). The subchronic oral toxicity of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these studies.

$ Repeated Dose 28-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3050; OECD Guideline 407)

No adverse effects were observed in four 28-day assays on mixtures containing phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester as a minor component. NOAELs of 1000 mg/kg/day were reported for rats exposed by oral gavage to CN-1985 in corn oil, NcendX P-30 in polyethylene glycol 400, or BPA:BDPP (vehicle not reported) (Safepharm, 1997f; Springborn, 2000; WIL Res. Labs., 1998b). No adverse effects were observed in male or female rats exposed to DVP 506 in the diet at concentrations as high as

20,000 ppm (FMC, 1997f). In this study the NOAELs were 1862 mg/kg/day for males and 1968 mg/kg/day for females.

$ 90-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3100; OECD Guideline 408)

No studies of this type were located.

$ **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**

No studies of this type were located.

Subchronic Dermal Toxicity (21/28-day or 90-day)

Conclusion:

The existing subchronic dermal toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No study was located that followed or was similar to the two guidelines listed below or otherwise addressed the subchronic dermal toxicity of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester.

$ 21/28-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3200 (OECD Guideline 410)
$ 90-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3250; OECD Guideline 411)

Subchronic Inhalation Toxicity (90-Day Inhalation Toxicity (OPPTS Harmonized Guideline 870.3250 (OECD Guideline 411))

Conclusion:

The existing data were judged inadequate to meet the endpoint

Basis for Conclusion:

No study was located that followed or was similar to the guideline or otherwise addressed the subchronic inhalation toxicity of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester.

REPRODUCTIVE TOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No study was located that followed or was similar to the three guidelines listed below or otherwise addressed the reproductive toxicity of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester.

- **Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)**
- **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**
- **Reproduction and Fertility Effects (OPPTS Harmonized Guideline 870.3800; OECD Guideline 416)**

DEVELOPMENTAL TOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint

Basis for Conclusion:

The only available developmental toxicity data were from a guideline study on a commercial mixture (Fyrolflex RDP) containing unreported amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester as a minor component. NOAELs of 1000 mg/kg/day were reported in a prenatal developmental toxicity study in rats exposed by oral gavage to CN-1985 (WIL Res. Labs., 1998c, 1998d). The developmental toxicity of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from this study.

$ Prenatal Developmental Toxicity Study (OPPTS Harmonized Guideline 870.3700; OECD Guideline 414)

In range-finding and main guideline studies, no adverse treatment-related maternal or developmental effects were observed in rats exposed by oral gavage in corn oil to CN-1985 at doses as high as 1000 mg/kg/day on gestational days 6-19 (WIL Res. Labs., 1998c, 1998d). There were no treatment-related effects on maternal food consumption, body weight, uterine parameters, or the incidences of fetal malformations or variations. Clinical signs observed in dams during dosing were related to aversion of the taste of the test material.

$ Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)

No studies of this type were located.

$ Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)

No studies of this type were located.

CHRONIC TOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No study was located that followed or was similar to the two guidelines listed below or otherwise addressed the chronic toxicity of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester.

- **Chronic Toxicity (OPPTS Harmonized Guideline 870.4100; OECD Guideline 452)**
- **Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)**

CARCINOGENICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No study was located that followed or was similar to the two guidelines listed below or otherwise addressed the carcinogencity of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester.

- **Carcinogenicity (OPPTS Harmonized Guideline 870.4200; OECD Guideline 451)**
- **Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)**

NEUROTOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No neurotoxicity studies conforming to any of the following or similar guidelines were available for phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. In a 28-day oral (gavage) toxicity study, no adverse effects were noted in weekly neurotoxicological examinations of rats exposed to ≤1000 mg/kg/day NcendX P-30, an undefined mixture containing phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester as a probable minor component (Australia DHA, 2005; Springborn, 2000). The neurotoxicity of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from this study.

- **Acute and 28-Day Delayed Neurotoxicity of Organophosphorus Substances (OPPTS Harmonized Guideline 870.6100; OECD Guideline 418, 419)**
- **Neurotoxicity (Adult)**: **Neurotoxicity Screening Battery (OPPTS Harmonized Guideline 870.6200; OECD Guideline 424)**
- **Developmental Neurotoxicity: Developmental Neurotoxicity Study (OPPTS Harmonized Guideline 870.6300)**

Additional neurotoxicity studies:

- Schedule-Controlled Operant Behavior (mouse or rat) (OPPTS Harmonized Guideline 870.6500)
- Peripheral Nerve Function (rodent) (OPPTS Harmonized Guideline 870.6850)
- Sensory Evoked Potentials (rat, pigmented strain preferred) (OPPTS Harmonized Guideline 870.6855)

These studies may be indicated, for example, to follow up neurotoxic signs seen in other studies, or because of structural similarity of the substance to neurotoxicants that affect these endpoints. These studies may be combined with other toxicity studies.

Conclusion: These endpoints do not appear to be applicable to phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester..

Basis for Conclusion: Although there are no studies addressing these endpoints, there are no reliable data for phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester, and no structure-activity considerations, that indicate a current need for these follow-up studies.

IMMUNOTOXICITY (OPPTS Harmonized Guideline 870.7800)

***Conclusion*:**

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No study was located that followed the guideline or otherwise addressed the immunotoxicity of of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester.

GENOTOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available genotoxicity data were from studies (some conducted under guideline) on commercial mixtures containing unknown (NcendX P-30, CN-1985) or unreported minor amounts (BPA: BDPP, DVP 506) of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl)

oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. These mixtures elicited negative results in studies for gene mutation in bacteria, and chromosomal aberration in vitro and in vivo. The genotoxicity of the minor component cannot be determined from these studies.

Gene Mutation in Vitro:

- **Bacterial Reverse Mutation test (OPPTS Harmonized Guideline 870.5100; OECD Guideline 471)**

As described in detailed summaries of guideline studies, neither BPA:BDPP nor NcendX P-30 caused an increase in the revertant frequency of *Salmonella typhimurium* strains TA1535, TA1537, TA98 or TA100 or *Escherichia coli* WP2*uvr*A at concentrations as high as 5 mg/plate (Inveresk, 1999f; Safepharm, 1997g). As described in incomplete summaries, neither DVP 506, batch 676/79 nor CN-1985 caused an increase the mutation frequency in *Salmonella typhimurium* or *Escherichia coli* at concentrations as high as 5 mg/plate with or without metabolic activation (Covance Labs., 1997a; Microbiological Associates, 1995). The potential of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester to induce mutations in bacteria cannot be determined from these studies.

$ **In vitro Mammalian Cell Gene Mutation Test (OPPTS Harmonized Guideline 870.5300; OECD Guideline 476)**

No study of this type was located.

$ **Mitotic Gene Conversion in Saccharomyces cerevisiae (OPPTS Harmonized Guideline 870.5575)**

No study of this type was located.

Gene Mutation in Vivo

No study of this type was located.

Chromosomal Aberrations in Vitro

$ **In vitro Chromosome Aberration Test (OPPTS Harmonized Guideline 870.5375)**

Mixtures containing minor (DVP 506, batch 676/79) or unknown (CN-1985) amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester did not increase the incidence of chromosomal aberrations in human peripheral lymphocytes with or without metabolic activation (Covance Labs., 1997b; Huntingdon, 1998); the latter experiment was conducted under guideline. In addition, guideline chromosomal aberration studies on undefined mixtures with probable low amounts of this compound reported

negative results in Chinese hamster lung cells cultured with BPA:BDPP and Chinese hamster ovary cells cultured with NcendX P-30 (Inveresk, 2000a; Safepharm, 1997h). The potential of phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester to induce chromosomal aberrations in vitro cannot be determined from these studies.

Chromosomal Aberrations in Vivo

$ **Mammalian Erythrocyte Micronucleus Test (OPPTS Harmonized Guideline 870.5395; OECD Guideline 474)**

Negative results were reported for micronucleus assays conducted on undefined mixtures likely containing phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester as a minor component. No increase in the frequency of bone marrow erythrocyte micronuclei was observed in male or female mice given a single intraperitoneal injection of 1250-5000 mg/kg CN-1985 and examined after 24, 48 and 72 hours (MA BioServices, 1998). NcendX P-30 did not increase the frequency of micronucleus formation in male or female mice dosed at 2000 mg/kg by oral gavage in corn oil and examined after 48 hours (Inveresk, 2000b). The potential of the minor component phosphoric acid, bis[4-[1-[4-[(diphenoxy-phosphinyl) oxy]phenyl]-1-methylethyl]phenyl] phenyl ester to induce chromosomal aberrations cannot be determined from these studies.

DNA Damage and Repair

No study of this type was located.

Ecotoxicity

Acute Toxicity to Aquatic Organisms

Conclusion:

The currently available data are not adequate to satisfy the acute toxicity endpoints for fish, aquatic invertebrates, or algae.

Basis for Conclusion:

No pertinent acute toxicity studies with fish, aquatic invertebrates, or algae for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester were located that addressed the endpoints in the guidelines listed below.

- **Acute Toxicity to Freshwater and Marine Fish (OPPTS Harmonized Guideline 850.1075; OECD Guideline 203)**

Experimental fish LD_{50} values of >0.025 mg/L (Australia DHA, 2005), >100 mg/L (Great lakes, 2003c) and >500 mg/L (Great Lakes, 2003c) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the acute toxicity values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results. In addition, the experimental LD_{50} values are all much greater than the estimated water solubility for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester, suggesting no effect at saturation.

- **Acute Toxicity to Freshwater Invertebrates (OPPTS Harmonized Guideline 850.1010; OECD Guideline 202)**

Experimental daphnia magna EC_{50} values of >0.02 mg/L (Australia DHA, 2005), >0.034 mg/L (Australia DHA, 2005), and >100 mg/L (Great Lakes, 2003a) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the acute toxicity values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results. In addition, the experimental EC_{50} values are all much greater than the estimated water solubility for pure

phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester, suggesting no effect at saturation.

- **Acute Toxicity to Marine/Estuarine Invertebrates (OPPTS Harmonized Guideline 850.1035)**
- **Algal Toxicity (OPPTS Harmonized Guideline 850.5400; OECD Guideline 201)**

Experimental algal EC_{50} values of >0.02 mg/L (Australia DHA, 2005), and >100 mg/L (Great Lakes, 2003c) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the acute toxicity values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results. In addition, the experimental EC_{50} values are all much greater than the estimated water solubility for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester, suggesting no effect at saturation.

Chronic Toxicity to Aquatic Organisms

Conclusion:

The currently available data are not adequate to satisfy the chronic toxicity endpoints for fish or aquatic invertebrates.

Basis for Conclusion:

No pertinent chronic toxicity studies with fish or aquatic invertebrates for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester were located that addressed the endpoints in the guidelines listed below.

- **Chronic Toxicity to Freshwater and Marine Fish (OPPTS Harmonized Guideline 850.1400; OECD Guideline 210)**

Experimental fish NOEC values of 5 mg/L (Great Lakes, 2003a) and >100 mg/L (Great Lakes, 2003a) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the chronic toxicity values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results. In addition, the experimental NOEC values are all much greater than the

estimated water solubility for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester, suggesting no effect at saturation.

- **Chronic Toxicity to Freshwater Invertebrates (OPPTS Harmonized Guideline 850.1300; OECD Guideline 211)**

An experimental daphnia magna NOEC value of >5 mg/L (Great Lakes, 2003a) has been reported for a commercial mixture of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contains varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of this mixture is not specified and, therefore, the chronic toxicity value for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from this results. In addition, the experimental NOEC value is much greater than the estimated water solubility for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester, suggesting no effect at saturation.

- **Chronic Toxicity to Marine/Estuarine Invertebrates (OPPTS Harmonized Guideline 850.1350)**

<u>Acute and Subchronic Toxicity to Terrestrial Organisms</u>

Conclusion:

The currently available data are not adequate to satisfy the acute or subchronic toxicity endpoints for terrestrial organisms.

Basis for Conclusion:

No pertinent acute oral, acute dietary, or reproductive toxicity studies with birds and no subchronic toxicity studies with earthworms for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester were located that addressed the endpoints in the guidelines listed below.

- **Acute Oral Toxicity in Birds (OPPTS Harmonized Guideline 850.2100)**
- **Acute Dietary Toxicity in Birds (OPPTS Harmonized Guideline 850.2200; OECD Guideline 205)**
- **Reproductive Toxicity in Birds (OPPTS Harmonized Guideline 850.2300; OECD Guideline 206)**
- **Earthworm Subchronic Toxicity (OPPTS Harmonized Guideline 850.6200; OECD Guideline 207)**

An experimental earthworm NOEC value of 1,000 mg/L (Great Lakes, 2003c) has been reported for a commercial mixture of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contains varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of this mixture is not specified and, therefore, the chronic toxicity value for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from this results.

Physical/Chemical Properties

Phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester

CAS	83029-72-5
MF	$C_{60}H_{53}O_{12}P_3$
MW	1059.00
SMILES	c1ccccc1OP(Oc2ccccc2)(=O)Oc3ccc(cc3)C(C)(C)c4ccc(cc4)OP(=O)(Oc5ccccc5)Oc6ccc(cc6)C(C)(C)c7ccc(cc7)OP(=O)(Oc8ccccc8)Oc9ccccc9

Water Solubility (mg/L):

Conclusion:

The currently available data are not adequate to satisfy the water solubility endpoint.

Basis for Conclusion:

Experimental data for the water solubility of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental water solubility values ranging from <0.02 mg/L to 10 mg/L (Australia DHA, 2005; Chang Chun, no date; Great Lakes, 2003a, 2003b, 2003c) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the water solubility values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

Log K_{ow}:

Conclusion:

The currently available data are not adequate to satisfy the log K_{ow} endpoint.

Basis for Conclusion:

Experimental data for the log K_{ow} of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental log K_{ow} values ranging from 4.0 to >5.7 (Australia DOH, 2005; Great Lakes, 2003a, 2003b, 2003c; Wildlife International Ltd., 2002) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified in the experimental study details and, therefore, the log K_{ow} values for pure phosphoric acid, bis[4-[1-[4-

[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

Oxidation/Reduction:

Conclusion:

The currently available data are not adequate to satisfy the oxidation/reduction endpoint.

Basis for Conclusion:

No data is available for the oxidation/reduction endpoint.

Melting Point:

Conclusion:

The currently available data are not adequate to satisfy the melting point endpoint.

Basis for Conclusion:

Experimental data for the melting point of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental melting point values of 7 °C (Great Lakes, 2003a) and 8 °C (Akzo Noble, 1999; Great Lakes, 2003b) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the melting point values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

Boiling Point:

Conclusion:

The currently available data are not adequate to satisfy the boiling point endpoint.

Basis for Conclusion:

Experimental data for the boiling point of pure pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental boiling point values of >220 °C (Great Lakes, 2003a), >240-250 °C (Australia DOH, 2005) and >300 °C (Akzo Noble, 1999; Great Lakes, 2003b, 2003c), as well as an experimental decomposition temperatures of >350 °C (Great Lakes, 2003a) have been reported for commercial mixtures of phosphoric trichloride, reaction products

with bisphenol A and phenol (181028-79-5) which contain varying amounts of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the boiling point values for pure pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

Vapor Pressure (torr):

Conclusion:

The currently available data are not adequate to satisfy the vapor pressure endpoint.

Basis for Conclusion:

Experimental data for the vapor pressure of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental vapor pressure values ranging from $2.3x10^{-18}$ torr to 0.18 torr (Akzo Noble, 1999; Australia DOH, 2005; Chang Chun, no date; Great Lakes, 20031, 3002c) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the vapor pressure values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

Odor:

Conclusion:

The currently available data are not adequate to satisfy the odor endpoint.

Basis for Conclusion:

No data are available for the odor endpoint.

Oxidation/Reduction Chemical Incompatibility:

Conclusion:

The currently available data are not adequate to satisfy the oxidation/reduction chemical incompatibility endpoint.

Basis for Conclusion:

No data are available for the oxidation/reduction chemical incompatibility endpoint.

Flammability:

Conclusion:

The currently available data are not adequate to satisfy the flammability endpoint.

Basis for Conclusion:

Experimental data for the flammability of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental flammability values of >400 °C (Great Lakes, 2003a) and 625 °C (Australia DOH, 2005) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the flammability values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

Flash Point:

Conclusion:

The currently available data are not adequate to satisfy the flash point endpoint.

Basis for Conclusion:

Experimental data for the flash point of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental flash point values of >200 °C (Great Lakes, 2003a), >250 °C (Great Lakes, 2003c), 281 °C (Great Lakes, 2003a), >334 °C (Chang Chun, no date) and >360 °C (Australia DOH, 2005) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the flash point values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

Explodability:

Conclusion:

The currently available data are not adequate to satisfy the explodability endpoint.

Basis for Conclusion:

No data are available for the explodability endpoint.

Corrosion Characteristics:

Conclusion:

The currently available data are not adequate to satisfy the corrosion characteristics endpoint.

Basis for Conclusion:

No data are available for the corrosion characteristics endpoint.

pH:

Conclusion:

The currently available data are not adequate to satisfy the pH endpoint.

Basis for Conclusion:

No data are available for the pH endpoint.

UV/VIS Absorption:

Conclusion:

The currently available data are not adequate to satisfy the UV/Vis absorption endpoint.

Basis for Conclusion:

No data are available for the UV/Vis absorption endpoint.

Viscosity:

Conclusion:

The currently available data are not adequate to satisfy the viscosity endpoint.

Basis for Conclusion:

Experimental data for the viscosity of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental viscosity values of 100 cSt (Great Lakes, 2003c) and 5040 cps (Great Lakes, no date) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the viscosity values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

Density/Relative Density/Bulk Density:

Conclusion:

The currently available data are not adequate to satisfy the density endpoint.

Basis for Conclusion:

Experimental data for the density of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental density values ranging from 1.2576 g/cc to 1.26 g/cc (Australia DOH, 2005; Chang Chun, no date; Great Lakes, no date, 2003a, 2003c) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the density values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

Dissociation Constant in Water:

Conclusion:

The currently available data are not adequate to satisfy the dissociation constant in water endpoint.

Basis for Conclusion:

No data is available for the dissociation constant in water endpoint.

Henry's Law Constant:

Conclusion:

The currently available data are not adequate to satisfy the Henry's law constant endpoint.

Basis for Conclusion:

No data are available for the Henry's law constant endpoint.

Environmental Fate

Bioconcentration

Fish:

Conclusion:

The currently available data are not adequate to satisfy the fish bioconcentration endpoint.

Basis for Conclusion:

No data are available for the fish bioconcentration endpoint.

Daphnids:

Conclusion:

The currently available data are not adequate to satisfy the daphnid bioconcentration endpoint.

Basis for Conclusion:

No data are available for the daphnid bioconcentration endpoint.

Green Algae:

Conclusion:

The currently available data are not adequate to satisfy the green algae bioconcentration endpoint.

Basis for Conclusion:

No data are available for the green algae bioconcentration endpoint.

Oysters:

Conclusion:

The currently available data are not adequate to satisfy the oysters bioconcentration endpoint.

Basis for Conclusion:

No data are available for the oysters bioconcentration endpoint.

Earthworms:

Conclusion:

The currently available data are not adequate to satisfy the earthworm bioconcentration endpoint.

Basis for Conclusion:

No data are available for the earthworm bioconcentration endpoint.

Fish Metabolism:

Conclusion:

The currently available data are not adequate to satisfy the fish metabolism endpoint.

Basis for Conclusion:

No data are available for the fish metabolism endpoint.

Degradation

Photolysis in the Atmosphere:

Conclusion:

The currently available data are not adequate to satisfy the photolysis in the atmosphere endpoint.

Basis for Conclusion:

No data are available for the photolysis in the atmosphere endpoint.

Photolysis in Water:

Conclusion:

The currently available data are not adequate to satisfy the photolysis in water endpoint.

Basis for Conclusion:

No data are available for the photolysis in water endpoint.

Photolysis in Soil:

Conclusion:

The currently available data are not adequate to satisfy the photolysis in soil endpoint.

Basis for Conclusion:

No data are available for the photolysis in soil endpoint.

Aerobic Biodegradation:

Conclusion:

The currently available data are not adequate to satisfy the aerobic biodegradation endpoint.

Basis for Conclusion:

Experimental data for the aerobic biodegradation of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental aerobic biodegradation values of 21.5% and 15.84% in 29 days in activated sludge (Great Lakes, 2003a), and 2% in 28 days in sewage sludge (Australia DOH, 2005) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the aerobic biodegradation values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

Anaerobic Biodegradation:

Conclusion:

The currently available data are not adequate to satisfy the anaerobic biodegradation endpoint.

Basis for Conclusion:

No data are available for the anaerobic biodegradation endpoint.

Porous Pot Test:

Conclusion:

The currently available data are not adequate to satisfy the porous pot test endpoint.

Basis for Conclusion:

No data are available for the porous pot test endpoint.

Pyrolysis:

Conclusion:

The currently available data are not adequate to satisfy the pyrolysis endpoint.

Basis for Conclusion:

No data are available for the pyrolysis endpoint.

Hydrolysis as a Function of pH:

Conclusion:

The currently available data are not adequate to satisfy the hydrolysis as a function of pH endpoint.

Basis for Conclusion:

Experimental data for the hydrolysis as a function of pH of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental hydrolysis half-life values of between 1 day and 1 year at pHs 4, 7 and 9 (Great Lakes, 2003a) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and

phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the hydrolysis values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

Sediment/Water Biodegradation:

Conclusion:

The currently available data are not adequate to satisfy the sediment/water biodegradation endpoint.

Basis for Conclusion:

Experimental data for the sediment/water biodegradation of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental sediment/water biodegradation DT(50) values of 762 days for sandy loam and 537 days (Great Lakes, 2003a) for sandy silt loam have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the sediment/water biodegradation values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

Soil Biodegradation with Product Identification:

Conclusion:

The currently available data are not adequate to satisfy the soil biodegradation endpoint.

Basis for Conclusion:

Experimental data for the soil biodegradation of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental soil biodegradation studies showing no significant degradation after 120 days (Great Lakes, 2003a) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the soil biodegradation values for pure phosphoric acid, bis[4-[1-[4-

[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

Indirect Photolysis in Water:

Conclusion:

The currently available data are not adequate to satisfy the indirect photolysis in water endpoint.

Basis for Conclusion:

No data are available for the indirect photolysis in water endpoint.

Sediment/Soil Adsorption/Desorption:

Conclusion:

The currently available data are not adequate to satisfy the sediment/soil adsorption/desorption endpoint.

Basis for Conclusion:

Experimental data for the sediment/soil adsorption/desorption of pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester are not reported in publicly available literature. Experimental sediment/soil adsorption/desorption log K_{oc} values of >5.4 (Great Lakes, 2003a) and 6.0-18.0 (Australia DOH, 2005) have been reported for commercial mixtures of phosphoric trichloride, reaction products with bisphenol A and phenol (181028-79-5) which contain varying amounts of phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the sediment/soil adsorption/desorption values for pure phosphoric acid, bis[4-[1-[4-[(diphenoxyphosphinyl)oxy]phenyl]-1-methylethyl]phenyl] phenyl ester cannot be determined from these results.

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Flame Retardant Alternative WS-3:
Phosphoric acid, 1,3-phenylene tetraphenyl ester
[Synonym: Resorcinol bis(diphenylphosphate)]
57583-54-7

Hazard Review

Phosphoric acid, 1,3-phenylene tetraphenyl ester
Existing Data Summary Table – Human Health Endpoints

T= Endpoint characterized by existing data * = Data available but not adequate	Ψ = Endpoint not applicable

Acute Toxicity	
Oral	
Dermal	
Inhalation	
Eye irritation	
Dermal irritation	
Skin sensitization	
Subchronic Toxicity	
28-Day oral	
90-Day oral	
Combined repeated dose with reproduction/ developmental toxicity screen	
21/28-Day dermal	
90-Day dermal	
28-Day inhalation	
90-Day inhalation	
Reproductive Toxicity	
Reproduction/ developmental toxicity screen	
Combined repeated dose with reproduction/ developmental toxicity screen	
Reproduction and fertility effects	

Developmental Toxicity	
Reproduction/ developmental toxicity screen	
Combined repeated dose with reproduction/ developmental toxicity screen	
Prenatal developmental	
Chronic Toxicity	
Chronic toxicity (two species)	
Combined chronic toxicity/ carcinogenicity	
Carcinogenicity	
Carcinogenicity (rat and mouse)	
Combined chronic toxicity/ carcinogenicity	

Neurotoxicity	
Acute and 28-day delayed neurotoxicity of organophosphorus substances (hen)	
Neurotoxicity screening battery (adult)	
Developmental neurotoxicity	
Additional neurotoxicity studies	
Immunotoxicity	
Immunotoxicity	
Genotoxicity	
Gene mutation in vitro	
Gene mutation in vivo	
Chromosomal aberrations in vitro	
Chromosomal aberrations in vivo	
DNA damage and repair	
Other	

Phosphoric acid, 1,3-phenylene tetraphenyl ester:
Existing Data Summary Table – Properties, Fate, and Ecotoxicity

T= Endpoint characterized by existing data * = Data available but not adequate	Ψ = Endpoint not applicable

P/Chem Properties	
Water solubility	
Octanol/water partition coefficient	
Oxidation/reduction	
Melting point	
Boiling point	
Vapor pressure	
Odor	
Oxidation/reduction chemical incompatibility	
Flammability	
Explodability	
Corrosion characteristics	
pH	
UV/visible absorption	
Viscosity	
Density/relative density/bulk density	
Dissociation constant in water	
Henry's Law constant	

Environmental Fate	
Bioconcentration	
Fish	
Daphnids	
Green algae	
Oysters	
Earthworms	
Metabolism in fish	
Degradation and Transport	
Photolysis, atmosphere	
Photolysis, water	
Photolysis in soil	
Aerobic biodegradation	
Anaerobic biodegradation	
Porous pot test	
Pyrolysis	
Hydrolysis as a function of pH	
Sediment/water biodegradation	
Soil biodegradation w/ product identification	
Indirect photolysis in water	
Sediment/soil adsorption/desorption	

Ecotoxicity	
Aquatic Toxicity	
Fish acute LC50	
Daphnia acute EC50	
Mysid shrimp acute LC50	
Green algae EC50, NOAEC, LOAEC	
Fish chronic NOAEL, LOAEC	
Daphnia chronic NOAEC, LOAEC	
Mysid shrimp chronic NOAEC, LOAEC	
Sediment organisms	
Terrestrial Organism Toxicity	
Bird LD50 (two species)	
Bird LC50 (two species)	
Bird reproduction	
Earthworm subchronic EC50, LC50, NOAEC, LOAEC	

Chemical Identity

Phosphoric acid, 1,3-phenylene tetraphenyl ester

Synonym	Resorcinol bis(diphenylphosphate) [RDP]
CAS	57583-54-7
MF	$C_{30}H_{24}O_8P_2$
MW	574.47
SMILES	c1ccccc1OP(Oc2ccccc2)(=O)Oc3cccc(c3)OP(=O)(Oc4ccccc4)Oc5ccccc5

Human Health Endpoints

The OPPTS Harmonized Test Guidelines are the preferred criteria for study adequacy, but the corresponding OECD Guidelines are also considered. The available studies generally conformed to these guidelines as well as Good Laboratory Practice guidelines. Studies that were published in a foreign language, or that were not readily available, and that were not critical to the hazard assessment were not retrieved.

The relevance of health effects studies in laboratory animals to humans needs to be considered in the context of anticipated human exposure patterns. For example, adverse effect levels measured following bolus exposure in oral gavage studies in animals may not directly pertain to human exposures from drinking water in which intakes occur over a longer time period during a day. The more gradual intakes are less likely to overwhelm detoxification processes than bolus delivery.

No studies were located on the effect of pure phosphoric acid, 1,3-phenylene tetraphenyl ester on human health endpoints, but some data were located for commercial products (CR-733-S and Fyrolflex RDP) characterized as phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (CAS No. 125997-21-9) and containing variable amounts of the compound. No information was provided on the composition of CR-733-S or Fyrolflex RDP used in the available human health studies. Henrich et al. (2000a) reported that Fyrolflex RDP may contain 65-80% phosphoric acid, 1,3-phenylene tetraphenyl ester, along with 15-30% higher oligomers and less than 5% triphenyl phosphate. Thus, it is possible that phosphoric acid, 1,3-phenylene tetraphenyl ester made a significant contribution to the toxicity elicited by Fyrolflex RDP in these studies.

ACUTE TOXICITY

Acute Oral Toxicity (OPPTS Harmonized Guideline 870.1100; OECD Guidelines 425, 420, 423, 401).

Conclusion:

The existing acute oral toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available acute oral toxicity data were guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP). Neither CR-733-S (RDP content unknown) nor Fyrolflex RDP (possibly 65-80% RDP) caused mortality in male or female rats given 5000 mg/kg by oral gavage (IIT Res. Inst., 1994a; RCC Notox BV, 1989a). No clinical signs of toxicity and no adverse effects on body weight gain or necropsy findings were observed in these studies. These results suggest that the acute oral lethality of phosphoric acid, 1,3-phenylene tetraphenyl ester may be low.

Acute Dermal Toxicity (OPPTS Harmonized Guideline 870.1200; OECD Guideline 402)

Conclusion:

The existing acute dermal toxicity data were judged inadequate to meet the endpoint.

***Basis for Conclusion*:**

The only available acute dermal toxicity data were guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP). Neither CR-733-S (RDP content unknown) nor Fyrolflex RDP (possibly 65-80% RDP) caused mortality in male or female rats exposed for 24 hours dermally at 2000 mg/kg (IIT Res. Inst., 1994b; RCC Notox BV, 1989b). Neither substance adversely affected body weight gain or necropsy findings. No clinical signs were observed following treatment with Fyrolflex RDP, but all rats exposed to CR-733-S experienced lethargy during the day of exposure. These results suggest that the acute dermal lethality of phosphoric acid, 1,3-phenylene tetraphenyl ester may be low.

Acute Inhalation Toxicity (OPPTS Harmonized Guideline 870.1300 (OECD Guideline 403)

Conclusion:

The existing acute inhalation toxicity data were judged inadequate to meet the endpoint..

Basis for Conclusion:

The only available acute inhalation toxicity data were guideline studies on aerosolized commercial mixtures containing unreported amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP). Neither CR-733-S (RDP content unknown) nor Fyrolflex RDP (possibly 65-80% RDP) caused mortality in male or female rats exposed nose-only for 4 hours to respirable aerosols at concentrations of 4140 or 4860 mg/m^3, respectively (IIT Res. Inst., 1994c; RCC Notox BV, 1989c). No adverse effects were noted on body weight gain or necropsy findings in either study. Clinical signs exhibited by rats exposed to Fyrolflex RDP included ptosis, salivation and discharge around the eyes and nose, whereas rats exposed to CR-733-S

exhibited agitation during exposure, and apathy, hunched posture, labored respiration and piloerection in the 48 hours after exposure. These results suggest that the acute inhalation lethality of phosphoric acid, 1,3-phenylene tetraphenyl ester may be low.

Acute Eye Irritation (OPPTS Harmonized Guideline 870.2400; OECD Guideline 405)

Conclusion:

The existing eye irritation data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available acute eye irritation data were from a guideline study on a commercial mixture (CR-733-S) containing unreported amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP). Application of 0.1 mL CR-733-S to the eyes of rabbits, elicited lacrimation in 3/3 animals on the first day, but no effects on the cornea or iris (RCC Notox BV, 1989d). One rabbit exhibited reddening of the conjunctiva of the eyelid during the first hour and then slight chemosis, which resolved within 24 hours. This experiment resulted in a Draize score of 3.3, indicating CR-733-S was minimally irritating to the eyes. The results suggest that phosphoric acid, 1,3-phenylene tetraphenyl ester may be minimally irritating to the eyes.

Acute Dermal Irritation (OPPTS Harmonized Guideline 870.2500; OECD Guideline 404)

Conclusions:

The existing acute dermal irritation data were judged inadequate to meet the endpoint.

Basis for Conclusions:

The only available acute dermal irritation data were from a guideline study on a commercial mixture (CR-733-S) containing unreported amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP). No erythema or edema was observed on rabbit skin at any time during the three days following a 4-hour application of 0.5 mL CR-733-S (RCC Notox BV, 1989e). The skin irritation Draize score in this study was 0. The results suggest that the potential for phosphoric acid, 1,3-phenylene tetraphenyl ester to cause acute dermal irritation may be low.

Skin Sensitization (OPPTS Harmonized Guideline 870.2600; OECD Guideline 429)

Conclusion:

The existing skin sensitization data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available skin sensitization data were from a guideline study on a commercial mixture (CR-733-S) containing unreported amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP). There was no sensitization reaction in guinea pigs that were first induced by intradermal injection with 2.5% (w/w) CR-733-S in propylene glycol and later challenged with a topical application of 100% CR-733-S (RCC Notox BV, 1989f). The skin sensitization score in this study was 0. The results suggest that the potential for phosphoric acid, 1,3-phenylene tetraphenyl ester to induce skin sensitization may be low.

SUBCHRONIC TOXICITY

The only available subchronic toxicity data were from guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP).

Oral exposure to high concentrations of RDP-containing mixtures in the diet resulted in reduced body weights because of lower palatability (Henrich et al., 2000b). Developmental effects in the dietary study therefore appear to be related to the effect of palatability on maternal nutrition and not to direct chemical toxicity on the fetus (Henrich et al., 2000b). Increased liver weight is a common finding in subchronic oral toxicity studies, but the lack of effect on serum enzymes (ALT, AST) or histopathology other than hepatocellular hypertrophy, suggests that enlargement of the liver is adaptive, a consequence of increased metabolic activity in the liver (Arthur D. Little Inc., 1989; Sherwood et al., 2000; Henrich et al., 2000b). Such hepatic effects are therefore not considered adverse for subchronic durations, but uncertainty remains as to whether chronic-duration exposure would result in the progression to hepatic disease.

The presence of higher molecular weight oligomers in the mixture tested in the inhalation study (Henrich et al., 2000a), may have exacerbated toxicity, since alveolar histiocytosis apparently developed as a reaction to the accumulation of water-insoluble foreign material in the lung. Additional testing would be needed to determine whether such effects would be observed for pure phosphoric acid, 1,3-phenylene tetraphenyl ester.

Subchronic Oral Toxicity (28-day, 90-day, or combined with reproductive/developmental)

Conclusion:

The existing subchronic oral toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available subchronic oral toxicity data were from guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP). These studies reported NOAEL values in the range of (1000-5000 mg/kg/day), (Arthur D. Little Inc., 1989; Henrich et al., 2000b; Sherwood et al., 2000). It is uncertain whether pure

phosphoric acid, 1,3-phenylene tetraphenyl ester would result in higher or lower NOAELs than observed in the studies on the mixtures.

- **Repeated Dose 28-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3050; OECD Guideline 407)**

A NOAEL of 1000 mg/kg/day was reported for rats exposed under guideline by oral gavage to CR-733-S (RDP content unknown) in corn oil for 28 days (Arthur D. Little, 1989). This study reported increases in absolute and relative liver weights in male and female rats, but in the absence of histopathology or biologically significant increases in plasma AST or ALT levels, these hepatic findings are not considered adverse.

In a specialized test of immunotoxicity of Fyrolflex RDP (possibly 65-80% RDP), no adverse effects on survival, body weight or a battery of immune function tests were observed in mice exposed by oral gavage (undiluted) at doses as high as 5000 mg/kg/day for 28 days (Sherwood et al., 2000). Activity levels of plasma pseudocholinesterase, a monocyte enzyme, were reduced in treated mice, but this finding is of doubtful toxicological significance except as a marker of gastrointestinal absorption of the test material. This study does not completely satisfy the guideline for a 28-day toxicity assay, because histological examinations were limited to organs associated with immune function.

- **90-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3100; OECD Guideline 408)**

No study was located that evaluated the oral toxicity of pure phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP) in a standard 90-day assay. The only similar study was a specialized two-generation reproductive toxicity assay in rats exposed to Fyrolflex RDP (possibly 65-80% RDP) at dietary concentrations as high as 20,000 ppm for more than 13 weeks (Henrich et al., 2000b). NOAELs of 1203 mg/kg/day for males and 1305 mg/kg/day for females were reported for developmental and reproductive endpoints at the highest dietary concentration. Reduced body weight gain in treated rats, as well as slight delays in postnatal developmental landmarks in offspring at 10,000 and 20,000 ppm, were attributed to reduced food consumption associated with lower palatability of treated feed. Increases in liver weight and slight hepatocellular hypertrophy, are considered to be adaptive and not adverse. This study does not fully conform to the guideline for a 90-day study because histopathological examinations were limited to the liver and reproductive organs.

- **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**

No studies of this type were located.

Subchronic Dermal Toxicity (21/28-day or 90-day)

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No study was located that followed or was similar to the two guidelines listed below or otherwise addressed the subchronic dermal toxicity of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP).

- **21/28-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3200 (OECD Guideline 410)**
- **90-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3250; OECD Guideline 411)**

Subchronic Inhalation Toxicity (28-day or 90-day)

Conclusion:

The existing data were judged inadequate to meet the endpoint

Basis for Conclusion:

The only available subchronic inhalation toxicity data were from a guideline study on a commercial mixture containing unreported amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP). A LOAEL of 500 mg/m^3 was reported for lung effects in rats exposed to Fyrolflex RDP (possibly 65-80% RDP) for 28 days according to OECD Guideline 412 (Henrich et al., 2000a). (OPPTS does not have a guideline for a subchronic inhalation toxicity study of that duration.) The extent to which phosphoric acid, 1,3-phenylene tetraphenyl ester or higher molecular weight oligomers in the mixture contributed to toxicity is uncertain.

- **28-Day Inhalation Toxicity (OECD Guideline 412)**

A NOAEL of 100 mg/m^3 and a LOAEL of 500 mg/m^3 were reported for lung histopathology (alveolar histiocytosis) in rats exposed nose-only to respirable aerosols of Fyrolflex RDP for 6

hours/day, 5 days/week for 4 weeks (Henrich et al., 2000a). In rats exposed at 2000 mg/m^3 and examined after a 60 day recovery period, the lung pathology had progressed to chronic inflammation, despite the cessation of treatment. The lung effects were attributed to the accumulation of unabsorbed water-insoluble foreign matter. It is uncertain whether pure phosphoric acid, 1,3-phenylene tetraphenyl ester would have resulted in higher or lower NOAEL values compared to the mixture.

- **90-Day Inhalation Toxicity (OPPTS Harmonized Guideline 870.3250 (OECD Guideline 411)**

No study of this type was located for pure RDP or mixtures containing RDP.

REPRODUCTIVE TOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available reproductive toxicity data were from a guideline study on a commercial mixture containing unreported amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP). NOAELs exceeding 1000 mg/kg/day were reported in a two-generation assay in rats exposed to Fyrolflex RPD (possibly 65-80% RDP) in the diet (Henrich et al., 2000b). The results suggest that the reproductive toxicity of phosphoric acid, 1,3-phenylene tetraphenyl may be low.

- **Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)**

No study of this type was located for RDP or mixtures containing RDP.

- **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**

No study of this type was located for RDP or mixtures containing RDP.

- **Reproduction and Fertility Effects (OPPTS Harmonized Guideline 870.3800; OECD Guideline 416)**

In a guideline two-generation assay in rats exposed to Fyrolflex RDP (possibly 65-80% RDP) at dietary concentrations as high as 20,000 ppm for more than 13 weeks, NOAELs of 1203 mg/kg/day for males and 1305 mg/kg/day for females were reported for developmental and

reproductive endpoints (Henrich et al., 2000b). There were no treatment-related effects on estrus cycles, vaginal cytology, or sperm parameters and no effect on reproductive organ weights or histology. Reductions in pup body weight, as well as slight delays in postnatal developmental landmarks (vaginal opening and preputial separation) in treated offspring compared to controls, were attributed to reduced feed intake because of an initial aversion to the taste in lactating dams at 10,000 and 20,000 ppm. The observed effects appeared to be related to feed palatability rather than direct toxicity to the fetus.

DEVELOPMENTAL TOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint

Basis for Conclusion:

The only available developmental toxicity data were from a guideline study on a commercial mixture containing unreported amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP). A NOAEL of 1000 mg/kg/day was reported in a prenatal developmental toxicity study in rabbits exposed by oral gavage to Fyrolflex RDP (possibly 65-80% RDP) (Ryan et al., 2000). The results suggest that the developmental toxicity of phosphoric acid, 1,3-phenylene tetraphenyl ester may be low.

- **Prenatal Developmental Toxicity Study (OPPTS Harmonized Guideline 870.3700; OECD Guideline 414)**

No adverse treatment-related maternal or developmental effects were observed in rabbits exposed by oral gavage in corn oil to Fyrolflex RDP at doses as high as 1000 mg/kg/day on gestational days 6-28 (Ryan et al., 2000). This study evaluated maternal food consumption, body weight, and weights of uterus, liver, kidney and spleen. No significant dose-related increases were observed in the incidences of external, skeletal or visceral malformations in fetuses.

- **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**

No studies of this type were located.

- **Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)**

No studies of this type were located.

CHRONIC TOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No chronic duration toxicity studies were located for pure phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP) or mixtures containing RDP.

- **Chronic Toxicity (OPPTS Harmonized Guideline 870.4100; OECD Guideline 452)**

No studies of this type were located.

- **Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)**

No studies of this type were located.

CARCINOGENICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No carcinogenicity studies were located for pure phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP) or mixtures containing RDP.

- **Carcinogenicity (OPPTS Harmonized Guideline 870.4200; OECD Guideline 451)**

No studies of this type were located.

- **Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)**

No studies of this type were located.

NEUROTOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No neurotoxicity data were available for pure phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP) or mixtures with a defined RDP content. No clinical signs indicative of neurotoxicity were observed in rodents exposed to high doses of undefined mixtures containing RDP: <5000 mg/kg by acute oral toxicity (see above) (IIT Res. Inst., 1994a; RCC Notox BV, 1989a) or 1000 mg/kg/day in subchronic oral gavage studies (see above) (Arthur D. Little Inc., 1989; Sherwood et al., 2000). A cholinesterase assay in rats exposed to CR-733-S (RDP content unknown) reported no treatment-related clinical signs in female rats and suggested that the material does not penetrate the blood-brain barrier (T.P.S., 1989). The ability of pure phosphoric acid, 1,3-phenylene tetraphenyl ester to penetrate the blood-brain barrier is not known.

- **Acute and 28-Day Delayed Neurotoxicity of Organophosphorus Substances (OPPTS Harmonized Guideline 870.6100; OECD Guideline 418, 419)**

No studies of this type were located.

- **Neurotoxicity (Adult)**: **Neurotoxicity Screening Battery (OPPTS Harmonized Guideline 870.6200; OECD Guideline 424)**

No studies of this type were located.

- **Developmental Neurotoxicity: Developmental Neurotoxicity Study (OPPTS Harmonized Guideline 870.6300)**

No studies of this type were located.

Additional neurotoxicity studies:

- Schedule-Controlled Operant Behavior (mouse or rat) (OPPTS Harmonized Guideline 870.6500)
- Peripheral Nerve Function (rodent) (OPPTS Harmonized Guideline 870.6850)
- Sensory Evoked Potentials (rat, pigmented strain preferred) (OPPTS Harmonized Guideline 870.6855)

These studies may be indicated, for example, to follow up neurotoxic signs seen in other studies, or because of structural similarity of the substance to neurotoxicants that affect these endpoints. These studies may be combined with other toxicity studies.

Conclusion: These endpoints do not appear to be applicable to phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP).

Basis for Conclusion: Although there are no studies addressing these endpoints, there are no reliable data for phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP, and no structure-activity considerations, that currently indicate a need for these follow-up studies.

IMMUNOTOXICITY

***Conclusion*:**

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available immunotoxicity data were from a guideline study on a commercial mixture containing an unreported amount of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP). No immunotoxicity was observed in mice treated with Fyrolflex RDP (possibly 65-80% RDP) (Sherwood et al., 2000). These results suggest the possibility that the immunotoxicity of phosphoric acid, 1,3-phenylene tetraphenyl ester may be low.

- **Immunotoxicity (OPPTS Harmonized Guideline 870.7800)**

No adverse effects on survival, body weight, organs related to immune function (thymus and spleen), or results of a battery of immune function tests were observed in mice exposed by oral gavage to undiluted Fyrolflex RDP at doses as high as 5000 mg/kg/day for 28 days (Sherwood et al., 2000).

GENOTOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available genotoxicity data were from guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester (RDP). Undefined mixtures yielded negative results for gene mutation in bacteria, and for chromosomal aberration in vitro and in vivo. These results suggest the possibility that the genotoxicity of phosphoric acid, 1,3-phenylene tetraphenyl ester may be low.

Gene Mutation in Vitro:

- **Bacterial Reverse Mutation test (OPPTS Harmonized Guideline 870.5100; OECD Guideline 471)**

CR-733-S (RDP content unknown) did not increase the mutation frequency in *Salmonella typhimurium* or *Escherichia coli* at concentrations as high as 5 mg/plate with or without metabolic activation (Covance Labs., 1998); strains used in these studies were not reported in the secondary source (Akzo Nobel, 2001). With or without metabolic activation, Fyrolflex RDP (possibly 65-80% RDP) at concentrations as high as 5 mg/plate was not mutagenic in *S. typhimurium* strains TA98, TA100, TA1537 or TA1545 (RCC Notox BV, 1988a).

- **In vitro Mammalian Cell Gene Mutation Test (OPPTS Harmonized Guideline 870.5300; OECD Guideline 476)**

No study of this type was located.

- **Mitotic Gene Conversion in Saccharomyces cerevisiae (OPPTS Harmonized Guideline 870.5575)**

No study of this type was located.

Gene Mutation in Vivo

No study of this type was located.

Chromosomal Aberrations in Vitro

- **In vitro Chromosome Aberration Test (OPPTS Harmonized Guideline 870.5375)**

No increase in the incidence of chromosomal aberrations was observed in human peripheral lymphocytes cultured with or without metabolic activation in the presence of CR-733-S (RDP content unknown) at concentrations as high as 0.625 mg/mL (RC Notox BV, 1989g).

Chromosomal Aberrations in Vivo

- **Mammalian Erythrocyte Micronucleus Test (OPPTS Harmonized Guideline 870.5395; OECD Guideline 474)**

No increase in the incidence of erythrocyte micronuclei was observed in mice given 5000 mg/kg CR-733-S (RDP content unknown) by oral gavage (RCC Notox BV, 1988b).

DNA Damage and Repair

No study of this type was located.

Ecotoxicity

Acute Toxicity to Aquatic Organisms

Conclusion:

The currently available data are not adequate to satisfy the acute toxicity endpoints for fish, aquatic invertebrates, or algae.

Basis for Conclusion:

No pertinent acute toxicity studies with fish, aquatic invertebrates, or algae for pure phosphoric acid, 1,3-phenylene tetraphenyl ester were located that addressed the endpoints in the guidelines listed below.

- **Acute Toxicity to Freshwater and Marine Fish (OPPTS Harmonized Guideline 850.1075; OECD Guideline 203)**

Experimental fish LD_{50} values of 12.4 mg/L (Akzo Noble, 2001; Great Lakes, 2003) and >10,000 mg/L (Bayer, 2002) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the acute toxicity values for pure phosphoric acid, 1,3-phenylene tetraphenyl ester cannot be determined from these results. In addition, the experimental LD_{50} values are all much greater than the estimated water solubility for pure phosphoric acid, 1,3-phenylene tetraphenyl ester, suggesting no effect at saturation.

- **Acute Toxicity to Freshwater Invertebrates (OPPTS Harmonized Guideline 850.1010; OECD Guideline 202)**

Experimental daphnia magna EC_{50} values of 0.76 mg/L (Akzo Noble, 2001) and 178 mg/L (Bayer, 2002) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the acute toxicity values for pure phosphoric acid, 1,3-phenylene tetraphenyl ester cannot be determined from these results. In addition, the experimental EC_{50} values are all much greater than the estimated water solubility for pure phosphoric acid, 1,3-phenylene tetraphenyl ester, suggesting no effect at saturation.

- **Acute Toxicity to Marine/Estuarine Invertebrates (OPPTS Harmonized Guideline 850.1035)**
- **Algal Toxicity (OPPTS Harmonized Guideline 850.5400; OECD Guideline 201)**

Experimental algal EC_{50} values of 48.6 mg/L (Akzo Noble, 2001; Great Lakes, 2003) and >10,000 mg/L (Bayer, 2002) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the acute toxicity values for pure phosphoric acid, 1,3-phenylene tetraphenyl ester cannot be determined from these results. In addition, the experimental EC_{50} values are all much greater than the estimated water solubility for pure phosphoric acid, 1,3-phenylene tetraphenyl ester, suggesting no effect at saturation.

Chronic Toxicity to Aquatic Organisms

Conclusion:

The currently available data are not adequate to satisfy the chronic toxicity endpoints for fish or aquatic invertebrates.

Basis for Conclusion:

No pertinent chronic toxicity studies with fish or aquatic invertebrates were located that addressed the endpoints in the guidelines listed below.

- **Chronic Toxicity to Freshwater and Marine Fish (OPPTS Harmonized Guideline 850.1400; OECD Guideline 210)**
- **Chronic Toxicity to Freshwater Invertebrates (OPPTS Harmonized Guideline 850.1300; OECD Guideline 211)**
- **Chronic Toxicity to Marine/Estuarine Invertebrates (OPPTS Harmonized Guideline 850.1350)**

Acute and Subchronic Toxicity to Terrestrial Organisms

Conclusion:

The currently available data are not adequate to satisfy the acute or subchronic toxicity endpoints for terrestrial organisms.

Basis for Conclusion:

No pertinent acute oral, acute dietary, or reproductive toxicity studies with birds and no subchronic toxicity studies with earthworms were located that addressed the endpoints in the guidelines listed below.

- **Acute Oral Toxicity in Birds (OPPTS Harmonized Guideline 850.2100)**

- **Acute Dietary Toxicity in Birds (OPPTS Harmonized Guideline 850.2200; OECD Guideline 205)**
- **Reproductive Toxicity in Birds (OPPTS Harmonized Guideline 850.2300; OECD Guideline 206)**
- **Earthworm Subchronic Toxicity (OPPTS Harmonized Guideline 850.6200; OECD Guideline 207)**

Physical/Chemical Properties

Phosphoric acid, 1,3-phenylene tetraphenyl ester
CAS 57583-54-7
MF $C_{30}H_{24}O_8P_2$
MW 574.47
SMILES c1ccccc1OP(Oc2ccccc2)(=O)Oc3cccc(c3)OP(=O)(Oc4ccccc4)Oc5ccccc5

Water Solubility (mg/L):

Conclusion:

The currently available data are not adequate to satisfy the water solubility endpoint.

Basis for Conclusion:

Experimental data for the water solubility of pure phosphoric acid, 1,3-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental water solubility values of <10 mg/L (Akzo Noble, 2001) and 500 mg/L (Chang Chun, no date) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the water solubility values for pure phosphoric acid, 1,3-phenylene tetraphenyl ester cannot be determined from these results.

Log K_{ow}:

Conclusion:

The currently available data are not adequate to satisfy the log K_{ow} endpoint.

Basis for Conclusion:

Experimental data for the log K_{ow} of pure phosphoric acid, 1,3-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental log K_{ow} values of 4.93 (Wildlife International Ltd., 2003) and 3.9-4.8 (Washington State DOH, 2005) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified in the experimental study details and, therefore, the log K_{ow} values for pure phosphoric acid, 1,3-phenylene tetraphenyl ester cannot be determined from these results.

Oxidation/Reduction:

Conclusion:

The currently available data are not adequate to satisfy the oxidation/reduction endpoint.

Basis for Conclusion:

No data are available for the oxidation/reduction endpoint.

Melting Point:

Conclusion:

The currently available data are not adequate to satisfy the melting point endpoint.

Basis for Conclusion:

Experimental data for the melting point of pure phosphoric acid, 1,3-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental melting point values of -12 °C (Akzo Noble, 1998; Bayer, 2002; Kirk-Othmer, 2005), -13 °C (Great Lakes, 2003) and -16.7 °C (Akzo Noble, 1998) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the melting point values for pure phosphoric acid, 1,3-phenylene tetraphenyl ester cannot be determined from these results.

Boiling Point:

Conclusion:

The currently available data are not adequate to satisfy the boiling point endpoint.

Basis for Conclusion:

Experimental data for the boiling point of pure phosphoric acid, 1,3-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental boiling point values of 300 °C (UBA, 2001a, 2003), >300 °C (Akzo Noble, 1998; Bayer, 2002; UBA, 2001b.) and 38 °C at 138 Pa (UBA, 2001a, 2001b, 2003), as well as experimental decomposition temperatures of >300 °C (Great Lakes, 2003; UBA, 2001b) and >400 °C (Bayer, 2002) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the boiling

point values for pure phosphoric acid, 1,3-phenylene tetraphenyl ester cannot be determined from these results.

Vapor Pressure (torr):

Conclusion:

The currently available data are not adequate to satisfy the vapor pressure endpoint.

Basis for Conclusion:

Experimental data for the vapor pressure of pure phosphoric acid, 1,3-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental vapor pressure values of <0.075 torr at 38 °C (Akzo Noble, 2001) and 0.007 torr at 38 °C (UBA, 2001a, 2001b, 2003) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the vapor pressure values for pure phosphoric acid, 1,3-phenylene tetraphenyl ester cannot be determined from these results.

Odor:

Conclusion:

The currently available data are not adequate to satisfy the odor endpoint.

Basis for Conclusion:

No data are available for the odor endpoint.

Oxidation/Reduction Chemical Incompatibility:

Conclusion:

The currently available data are not adequate to satisfy the oxidation/reduction chemical incompatibility endpoint.

Basis for Conclusion:

No data are available for the oxidation/reduction chemical incompatibility endpoint.

Flammability:

Conclusion:

The currently available data are not adequate to satisfy the flammability endpoint.

Basis for Conclusion:

No data are available for the flammability endpoint.

Flash Point:

Conclusion:

The currently available data are not adequate to satisfy the flash point endpoint.

Basis for Conclusion:

Experimental data for the flash point of pure phosphoric acid, 1,3-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental flash point values of >240 °C (Chang Chun, no date) and 302 °C (Bayer, 2002) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the flash point values for pure phosphoric acid, 1,3-phenylene tetraphenyl ester cannot be determined from these results.

Explodability:

Conclusion:

The currently available data are not adequate to satisfy the explodability endpoint.

Basis for Conclusion:

No data are available for the explodability endpoint.

Corrosion Characteristics:

Conclusion:

The currently available data are not adequate to satisfy the corrosion characteristics endpoint.

Basis for Conclusion:

No data are available for the corrosion characteristics endpoint.

pH:

Conclusion:

The currently available data are not adequate to satisfy the pH endpoint.

Basis for Conclusion:

No data are available for the pH endpoint.

UV/VIS Absorption:

Conclusion:

The currently available data are not adequate to satisfy the UV/Vis absorption endpoint.

Basis for Conclusion:

No data are available for the UV/Vis absorption endpoint.

Viscosity:

Conclusion:

The currently available data are not adequate to satisfy the viscosity endpoint.

Basis for Conclusion:

Experimental data for the viscosity of pure phosphoric acid, 1,3-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental viscosity values of 240 mPas (Akzo Noble, 1998), 600 mPas (Akzo Noble, 1998), 500-700 mPas (Bayer, 2002) and 400-800 mPas (Great Lakes, 2003) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the viscosity values for pure phosphoric acid, 1,3-phenylene tetraphenyl ester cannot be determined from these results.

Density/Relative Density/Bulk Density:

Conclusion:

The currently available data are not adequate to satisfy the density endpoint.

Basis for Conclusion:

Experimental data for the density of pure phosphoric acid, 1,3-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental density values

ranging from 1.29 g/cc to 1.32 g/cc (Bayer, 2002; Chang Chun, no date; Great Lakes, 2003) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the density values for pure phosphoric acid, 1,3-phenylene tetraphenyl ester cannot be determined from these results.

Dissociation Constant in Water:

Conclusion:

The currently available data are not adequate to satisfy the dissociation constant in water endpoint.

Basis for Conclusion:

No data are available for the dissociation constant in water endpoint.

Henry's Law Constant:

Conclusion:

The currently available data are not adequate to satisfy the Henry's law constant endpoint.

Basis for Conclusion:

No data are available for the Henry's law constant endpoint.

Environmental Fate

Bioconcentration

Fish:

Conclusion:

The currently available data are not adequate to satisfy the fish bioconcentration endpoint.

Basis for Conclusion:

No data are available for the fish bioconcentration endpoint.

Daphnids:

Conclusion:

The currently available data are not adequate to satisfy the daphnid bioconcentration endpoint.

Basis for Conclusion:

No data are available for the daphnid bioconcentration endpoint.

Green Algae:

Conclusion:

The currently available data are not adequate to satisfy the green algae bioconcentration endpoint.

Basis for Conclusion:

No data are available for the green algae bioconcentration endpoint.

Oysters:

Conclusion:

The currently available data are not adequate to satisfy the oysters bioconcentration endpoint.

Basis for Conclusion:

No data are available for the oysters bioconcentration endpoint.

Earthworms:

Conclusion:

The currently available data are not adequate to satisfy the earthworm bioconcentration endpoint.

Basis for Conclusion:

No data are available for the earthworm bioconcentration endpoint.

Fish Metabolism:

Conclusion:

The currently available data are not adequate to satisfy the fish metabolism endpoint.

Basis for Conclusion:

No data are available for the fish metabolism endpoint.

Degradation

Photolysis in the Atmosphere:

Conclusion:

The currently available data are not adequate to satisfy the photolysis in the atmosphere endpoint.

Basis for Conclusion:

No data are available for the photolysis in the atmosphere endpoint.

Photolysis in Water:

Conclusion:

The currently available data are not adequate to satisfy the photolysis in water endpoint.

Basis for Conclusion:

No data are available for the photolysis in water endpoint.

Photolysis in Soil:

Conclusion:

The currently available data are not adequate to satisfy the photolysis in soil endpoint.

Basis for Conclusion:

No data are available for the photolysis in soil endpoint.

Aerobic Biodegradation:

Conclusion:

The currently available data are not adequate to satisfy the aerobic biodegradation endpoint.

Basis for Conclusion:

Experimental data for the aerobic biodegradation of pure phosphoric acid, 1,3-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental aerobic biodegradation values of 37% in 28 days and 66% after 56 days (Akzo Noble, 2001) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the aerobic biodegradation values for pure phosphoric acid, 1,3-phenylene tetraphenyl ester cannot be determined from these results.

Anaerobic Biodegradation:

Conclusion:

The currently available data are not adequate to satisfy the anaerobic biodegradation endpoint.

Basis for Conclusion:

No data are available for the anaerobic biodegradation endpoint.

Porous Pot Test:

Conclusion:

The currently available data are not adequate to satisfy the porous pot test endpoint.

Basis for Conclusion:

No data are available for the porous pot test endpoint.

Pyrolysis:

Conclusion:

The currently available data are not adequate to satisfy the pyrolysis endpoint.

Basis for Conclusion:

No data are available for the pyrolysis endpoint.

Hydrolysis as a Function of pH:

Conclusion:

The currently available data are not adequate to satisfy the hydrolysis as a function of pH endpoint.

Basis for Conclusion:

Experimental data for the hydrolysis as a function of pH of pure phosphoric acid, 1,3-phenylene tetraphenyl ester are not reported in publicly available literature. Experimental hydrolysis half-life values of 11 days at pH 4, 17 days at pH 7 and 21 days at pH 9 (Akzo Noble, 2001) and of 17 days at pH 7 (European Flame Retardants Association, no date) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, 1,3-phenylene tetraphenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the hydrolysis values for pure phosphoric acid, 1,3-phenylene tetraphenyl ester cannot be determined from these results.

Sediment/Water Biodegradation:

Conclusion:

The currently available data are not adequate to satisfy the sediment/water biodegradation endpoint.

Basis for Conclusion:

No data are available for the sediment/water biodegradation endpoint.

Soil Biodegradation with Product Identification:

Conclusion:

The currently available data are not adequate to satisfy the soil biodegradation with product identification endpoint.

Basis for Conclusion:

No data are available for the soil biodegradation with product identification endpoint.

Indirect Photolysis in Water:

Conclusion:

The currently available data are not adequate to satisfy the indirect photolysis in water endpoint.

Basis for Conclusion:

No data are available for the indirect photolysis in water endpoint.

Sediment/Soil Adsorption/Desorption:

Conclusion:

The currently available data are not adequate to satisfy the sediment/soil adsorption/desorption endpoint.

Basis for Conclusion:

No data are available for the sediment/soil adsorption/desorption endpoint.

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Flame Retardant Alternative WS-4:
Phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester
98165-92-5

Hazard Review

Phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester: Existing Data Summary Table – Human Health Endpoints

T= Endpoint characterized by existing data * = Data available but not adequate	Ψ = Endpoint not applicable

Acute Toxicity	
Oral	
Dermal	
Inhalation	
Eye irritation	
Dermal irritation	
Skin sensitization	
Subchronic Toxicity	
28-Day oral	
90-Day oral	
Combined repeated dose with reproduction/ developmental toxicity screen	
21/28-Day dermal	
90-Day dermal	
28-Day inhalation	
90-Day inhalation	
Reproductive Toxicity	
Reproduction/ developmental toxicity screen	
Combined repeated dose with reproduction/ developmental toxicity screen	
Reproduction and fertility effects	

Developmental Toxicity	
Reproduction/ developmental toxicity screen	
Combined repeated dose with reproduction/ developmental toxicity screen	
Prenatal developmental	
Chronic Toxicity	
Chronic toxicity (two species)	
Combined chronic toxicity/ carcinogenicity	
Carcinogenicity	
Carcinogenicity (rat and mouse)	
Combined chronic toxicity/ carcinogenicity	

Neurotoxicity	
Acute and 28-day delayed neurotoxicity of organophosphorus substances (hen)	
Neurotoxicity screening battery (adult)	
Developmental neurotoxicity	
Additional neurotoxicity studies	
Immunotoxicity	
Immunotoxicity	
Genotoxicity	
Gene mutation in vitro	
Gene mutation in vivo	
Chromosomal aberrations in vitro	
Chromosomal aberrations in vivo	
DNA damage and repair	
Other	

Phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester: Existing Data Summary Table – Properties, Fate, and Ecotoxicity

T= Endpoint characterized by existing data * = Data available but not adequate	Ψ = Endpoint not applicable

P/Chem Properties	
Water solubility	
Octanol/water partition coefficient	
Oxidation/reduction	
Melting point	
Boiling point	
Vapor pressure	
Odor	
Oxidation/reduction chemical incompatibility	
Flammability	
Explodability	
Corrosion characteristics	
pH	
UV/visible absorption	
Viscosity	
Density/relative density/bulk density	
Dissociation constant in water	
Henry's Law constant	

Environmental Fate	
Bioconcentration	
Fish	
Daphnids	
Green algae	
Oysters	
Earthworms	
Metabolism in fish	
Degradation and Transport	
Photolysis, atmosphere	
Photolysis, water	
Photolysis in soil	
Aerobic biodegradation	
Anaerobic biodegradation	
Porous pot test	
Pyrolysis	
Hydrolysis as a function of pH	
Sediment/water biodegradation	
Soil biodegradation w/ product identification	
Indirect photolysis in water	
Sediment/soil adsorption/desorption	

Ecotoxicity	
Aquatic Toxicity	
Fish acute LC50	
Daphnia acute EC50	
Mysid shrimp acute LC50	
Green algae EC50, NOAEC, LOAEC	
Fish chronic NOAEL, LOAEC	
Daphnia chronic NOAEC, LOAEC	
Mysid shrimp chronic NOAEC, LOAEC	
Sediment organisms	
Terrestrial Organism Toxicity	
Bird LD50 (two species)	
Bird LC50 (two species)	
Bird reproduction	
Earthworm subchronic EC50, LC50, NOAEC, LOAEC	

Chemical Identity

Phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester

CAS	98165-92-5
MF	C42H33O12P3
MW	822.64
SMILES	c1ccccc1OP(Oc2ccccc2)(=O)Oc3cccc(c3)OP(=O)(Oc4ccccc4)Oc5cccc(c5)OP(=O)(Oc6ccccc6)Oc7ccccc7

Human Health Endpoints

The OPPTS Harmonized Test Guidelines are the preferred criteria for study adequacy, but the corresponding OECD Guidelines are also considered. The available studies generally conformed to these guidelines as well as Good Laboratory Practice guidelines. Studies that were published in a foreign language, or that were not readily available, and that were not critical to the hazard assessment were not retrieved.

The relevance of health effects studies in laboratory animals to humans needs to be considered in the context of anticipated human exposure patterns. For example, adverse effect levels measured following bolus exposure in oral gavage studies in animals may not directly pertain to human exposures from drinking water in which intakes occur over a longer time period during a day. The more gradual intakes are less likely to overwhelm detoxification processes than bolus delivery.

No studies were located on the effect of pure phosphoric acid, bis[3-[(diphenoxyphosphinyl) oxy]phenyl] phenyl ester (CAS No. 98165-92-5) on human health endpoints, but some data were located for commercial products (CR-733S and Fyrolflex RDP) characterized as phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (CAS No. 125997-21-9) and containing unknown amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. No information was available as to the composition of CR-733S, but Henrich et al. (2000a) reported that Fyrolflex RDP may contain 15-30% of higher oligomers of phosphoric acid, 1,3-phenylene tetraphenyl ester (synonym: resorcinol bis(diphenyl phosphate); RDP), of which phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester would be a major fraction. Other components of Fyrolflex RDP are 65-80% (RDP; CAS No. 57583-54-7) and less than 5% triphenyl phosphate (CAS No. 115-86-6).

ACUTE TOXICITY

Acute Oral Toxicity (OPPTS Harmonized Guideline 870.1100; OECD Guidelines 425, 420, 423, 401).

Conclusion:

The existing acute oral toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only acute oral toxicity data were guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester as a minor component. Neither CR-733-S nor Fyrolflex RDP caused mortality in male or female rats given 5000 mg/kg by oral gavage (IIT Res. Inst., 1994a; RCC Notox BV, 1989a). No clinical signs of toxicity and no adverse effects on body weight gain or necropsy findings were observed in these studies. The acute oral lethality of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these studies.

Acute Dermal Toxicity (OPPTS Harmonized Guideline 870.1200; OECD Guideline 402)

Conclusion:

The existing acute dermal toxicity data were judged inadequate to meet the endpoint.

***Basis for Conclusion*:**

The only acute dermal toxicity data were guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester as a minor component. Neither CR 733-S nor Fyrolflex RDP caused mortality in male or female rats exposed for 24 hours dermally at 2000 mg/kg (IIT Res. Inst., 1994b; RCC Notox BV, 1989b). Neither substance adversely affected body weight gain or necropsy findings. No clinical signs were observed following treatment with Fyrolflex RDP, but all rats exposed to CR 733-S experienced lethargy during the day of exposure. The acute dermal lethality of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these studies.

Acute Inhalation Toxicity (OPPTS Harmonized Guideline 870.1300 (OECD Guideline 403)

Conclusion:

The existing acute inhalation toxicity data were judged inadequate to meet the endpoint..

Basis for Conclusion:

The only acute inhalation toxicity data were from guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester as a minor component. No mortality was observed in male or female rats exposed nose-only for 4 hours to respirable aerosols of CR 733-S or Fyrolflex RDP at concentrations of 4140 or 4860 mg/m^3, respectively (IIT Res. Inst., 1994c; RCC Notox BV, 1989c). No adverse effects were noted on body weight gain or necropsy findings in either study. Clinical signs exhibited by rats exposed to Fyrolflex RDP included ptosis, salivation and discharge around the eyes and nose, whereas rats exposed to CR 733-S exhibited agitation during exposure, and

apathy, hunched posture, labored respiration and piloerection in the 48 hours after exposure. The acute inhalation lethality of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these studies.

Acute Eye Irritation (OPPTS Harmonized Guideline 870.2400; OECD Guideline 405)

Conclusion:

The existing eye irritation data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only acute eye irritation data were from a guideline study on a commercial mixture containing unreported amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester as a minor component. Application of 0.1 mL CR-733-S to the eyes of rabbits, elicited lacrimation in 3/3 animals on the first day, but no effects on the cornea or iris (RCC Notox BV, 1989d). One rabbit exhibited reddening of the conjunctiva of the eyelid during the first hour and then slight chemosis, which resolved within 24 hours. This experiment resulted in a Draize score of 3.3, indicating CR-733-S was minimally irritating to the eyes. The potential for phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester to cause eye irritation cannot be determined from this study.

Acute Dermal Irritation (OPPTS Harmonized Guideline 870.2500; OECD Guideline 404)

Conclusions:

The existing dermal irritation data were judged inadequate to meet the endpoint.

Basis for Conclusions:

The only acute dermal irritation data were from a guideline study on a commercial mixture containing unreported amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester as a minor component. No erythema or edema was observed on rabbit skin at any time during the three days following a 4-hour application of 0.5 mL CR-733-S (RCC Notox BV, 1989e. The skin irritation Draize score in this study was 0. The potential of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester to cause skin irritation cannot be determined from this study.

Skin Sensitization (OPPTS Harmonized Guideline 870.2600; OECD Guideline 429)

Conclusion:

The existing skin sensitization data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only acute skin sensitization data were from a guideline study on a commercial mixture containing unreported amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester as a minor component. There was no sensitization reaction in guinea pigs that were first induced by intradermal injection with 2.5% (w/w) CR-733-S in propylene glycol and later challenged with a topical application of 100% CR-733-S (RCC Notox BV, 1989f). The skin sensitization score in this study was 0. The skin sensitization properties of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from this study.

SUBCHRONIC TOXICITY

The only subchronic toxicity data were from guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester as a minor component.

Oral exposure to high concentrations of undefined mixtures in the diet resulted in reduced body weights because of lower palatability (Henrich et al., 2000b). Developmental effects in the dietary study therefore appear to be related to the effect of palatability on maternal nutrition and not to direct chemical toxicity on the fetus (Henrich et al., 2000b). Increased liver weight is a common finding in subchronic oral toxicity studies, but the lack of effect on serum enzymes (ALT, AST) or histopathology other than hepatocellular hypertrophy, suggests that enlargement of the liver is adaptive, a consequence of increased metabolic activity in the liver (Arthur D. Little Inc., 1989; Henrich et al., 2000b; Sherwood et al., 2000;). Such hepatic effects are therefore not considered adverse for subchronic durations, but uncertainty remains as to whether chronic-duration exposure would result in the progression to hepatic disease. Given the lack of information about absorption through the gastrointestinal tract, the contribution of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester to these effects is uncertain.

In the subchronic inhalation study, the presence of higher molecular weight oligomers such as phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester is likely to have contributed to the toxicity of the tested mixture (Henrich et al., 2000a), since alveolar histiocytosis apparently developed as a reaction to the accumulation of water-insoluble foreign material in the lung.

Subchronic Oral Toxicity (28-day, 90-day, or combined with reproductive/developmental)

Conclusion:

The existing subchronic oral toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only subchronic oral toxicity data were from guideline studies on commercial mixtures containing unreported amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester as a minor component. These studies reported NOAEL values in the range of 1000-5000 mg/kg/day (Arthur D. Little Inc., 1989; Henrich et al., 2000b; Sherwood et al., 2000). The subchronic oral toxicity of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these studies.

$ Repeated Dose 28-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3050; OECD Guideline 407)

A NOAEL of 1000 mg/kg/day was reported for rats exposed under guideline by oral gavage to CR-733-S in corn oil for 28 days (Arthur D. Little Inc., 1989). This study reported increases in absolute and relative liver weights in male and female rats, but in the absence of histopathology or biologically significant increases in plasma AST or ALT levels, these hepatic findings are not considered adverse.

In a specialized test of the immunotoxicity of Fyrolflex RDP, no adverse effects on survival, body weight, or a battery of immune function tests were observed in mice exposed by oral gavage (undiluted) at doses as high as 5000 mg/kg/day for 28 days (Sherwood et al., 2000). Activity levels of plasma pseudocholinesterase, a monocyte enzyme, were reduced in treated mice, but this finding is of doubtful toxicological significance except as a marker of gastrointestinal absorption of the test material. This study does not completely satisfy the guideline for a 28-day toxicity assay, because histological examinations were limited to organs associated with immune function.

$ 90-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3100; OECD Guideline 408)

No study was located that evaluated the oral toxicity of pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester in a standard 90-day assay. The only similar study was a specialized two-generation reproductive toxicity assay in rats exposed for more than 13 weeks to dietary concentrations of ≤20,000 ppm Fyrolflex RDP containing phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester as a minor component. (Henrich et al., 2000b). NOAELs of 1203 mg/kg/day for males and 1305 mg/kg/day for females were reported for developmental and reproductive endpoints at the highest dietary concentration. Reduced body weight gain in treated rats, as well as slight delays in postnatal developmental landmarks in offspring at 10,000 and 20,000 ppm, were attributed to reduced food consumption associated with lower palatability of treated feed. Increases in liver weight and slight hepatocellular hypertrophy, are considered to be adaptive and not adverse. This study does not fully conform to the guideline for a 90-day study because histopathological examinations are limited to the liver and reproductive organs.

$ **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**

No studies of this type were located.

Subchronic Dermal Toxicity (21/28-day or 90-day)

Conclusion:

The existing subchronic dermal toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No study was located that followed or was similar to the two guidelines listed below or otherwise addressed the subchronic dermal toxicity of phosphoric acid, bis[3-[(diphenoxyphosphinyl) oxy]phenyl] phenyl ester.

$ 21/28-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3200 (OECD Guideline 410)
$ 90-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3250; OECD Guideline 411)

Subchronic Inhalation Toxicity (28-day or 90-day)

Conclusion:

The existing data were judged inadequate to meet the endpoint

Basis for Conclusion:

The only available subchronic inhalation toxicity data were from a guideline study on a commercial mixture containing unreported amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl) oxy]phenyl] phenyl ester as a minor component. A LOAEL of 500 mg/m^3 was reported in rats exposed for 28 days to Fyrolflex RDP according to OECD Guideline 412 (Henrich et al., 2000a). (OPPTS does not have a guideline for a subchronic inhalation toxicity study of that duration.) The contribution of phosphoric acid, bis[3-[(diphenoxyphosphinyl) oxy]phenyl] phenyl ester to inhalation toxicity is uncertain, since larger oligomers were also present in the mixture.

$ 28-Day Inhalation Toxicity (OECD Guideline 412)

A NOAEL of 100 mg/m^3 and a LOAEL of 500 mg/m^3 were reported for lung histopathology (alveolar histiocytosis) in rats exposed nose-only to respirable aerosols of Fyrolflex RDP for 6 hours/day, 5 days/week for 4 weeks (Henrich et al., 2000a). In rats exposed at 2000 mg/m^3 and examined after a 60 day recovery period, the lung pathology had progressed to chronic inflammation, despite the cessation of treatment. The lung effects were attributed to the accumulation of water-insoluble foreign matter.

$ 90-Day Inhalation Toxicity (OPPTS Harmonized Guideline 870.3250 (OECD Guideline 411)

No study of this type was located for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl) oxy]phenyl] phenyl ester or defined mixtures.

REPRODUCTIVE TOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available reproductive toxicity data were from a guideline study on a commercial mixture containing unreported amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl) oxy]phenyl] phenyl ester as a minor component. NOAELs exceeding 1000 mg/kg/day were reported in a two-generation assay in rats exposed to Fyrolflex RPD in the diet (Henrich et al., 2000b). The reproductive toxicity of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from this study.

$ Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)

No study of this type was located for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl) oxy]phenyl] phenyl ester or defined mixtures.

$ Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)

No study of this type was located for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl) oxy]phenyl] phenyl ester or defined mixtures.

$ Reproduction and Fertility Effects (OPPTS Harmonized Guideline 870.3800; OECD Guideline 416)

In a guideline two-generation assay, rats were exposed for more than 13 to dietary concentrations of ≤20,000 ppm Fyrolflex RDP containing phosphoric acid, bis[3-[(diphenoxyphosphinyl) oxy]phenyl] phenyl ester as a minor component (Henrich et al., 2000b). NOAELs of 1203 mg/kg/day for males and 1305 mg/kg/day for females were reported for developmental and reproductive endpoints. There were no treatment-related effects on estrus cycles, vaginal cytology, or sperm parameters and no effect on reproductive organ weights or histology. Reductions in pup body weight, as well as slight delays in postnatal developmental landmarks (vaginal opening and preputial separation) in offspring compared to controls, were attributed to reduced feed intake because of an initial aversion to the taste in lactating dams at 10,000 and 20,000 ppm. The observed effects appeared to be related to feed palatability rather than direct toxicity to the fetus.

DEVELOPMENTAL TOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint

Basis for Conclusion:

The only available developmental toxicity data were from a guideline study on a commercial mixture (Fyrolflex RDP) containing unreported amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl) oxy]phenyl] phenyl ester as a minor component (Ryan et al., 2000). The developmental toxicity of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from this study.

$ Prenatal Developmental Toxicity Study (OPPTS Harmonized Guideline 870.3700; OECD Guideline 414)

No adverse treatment-related maternal or developmental effects were observed in rabbits exposed by oral gavage in corn oil to Fyrolflex RDP at doses as high as 1000 mg/kg/day on gestational days 6-28 (Ryan et al., 2000). This study evaluated maternal food consumption, body weight, and weights of uterus, liver, kidney and spleen. No significant dose-related increases were observed in the incidences of external, skeletal or visceral malformations in fetuses.

$ Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)

No studies of this type were located.

$ Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)

No studies of this type were located.

CHRONIC TOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No chronic duration toxicity studies were located for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester or defined mixtures.

$ Chronic Toxicity (OPPTS Harmonized Guideline 870.4100; OECD Guideline 452)

No studies of this type were located.

$ Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)

No studies of this type were located.

CARCINOGENICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No chronic duration toxicity studies were located for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester or defined mixtures.

$ Carcinogenicity (OPPTS Harmonized Guideline 870.4200; OECD Guideline 451)

No studies of this type were located.

$ Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)

No studies of this type were located.

NEUROTOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No neurotoxicity data were available for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl) oxy]phenyl] phenyl ester or defined mixtures. No clinical signs indicative of neurotoxicity were observed in rodents exposed to high doses of undefined mixtures containing phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester as a minor component: <5000 mg/kg by acute oral toxicity (see above) (IIT Res. Inst., 1994a; RCC Notox BV, 1989a) or 1000 mg/kg/day in subchronic oral gavage studies (see above) (Arthur D. Little Inc., 1989; Sherwood et al., 2000). A cholinesterase assay in rats exposed to the mixture CR-733-S reported no treatment-related clinical signs in female rats and suggested that the material does not penetrate the blood-brain barrier (T.P.S, 1989). The neurotoxicity of phosphoric acid, bis[3-[(diphenoxyphosphinyl) oxy]phenyl] phenyl ester cannot be determined from these studies, as the ability of this material to penetrate the blood-brain barrier is not known.

$ Acute and 28-Day Delayed Neurotoxicity of Organophosphorus Substances (OPPTS Harmonized Guideline 870.6100; OECD Guideline 418, 419)

No studies of this type were located.

$ Neurotoxicity (Adult): **Neurotoxicity Screening Battery (OPPTS Harmonized Guideline 870.6200; OECD Guideline 424)**

No studies of this type were located.

- **Developmental Neurotoxicity: Developmental Neurotoxicity Study (OPPTS Harmonized Guideline 870.6300)**

No studies of this type were located.

Additional neurotoxicity studies:

- Schedule-Controlled Operant Behavior (mouse or rat) (OPPTS Harmonized Guideline 870.6500)
- Peripheral Nerve Function (rodent) (OPPTS Harmonized Guideline 870.6850)
- Sensory Evoked Potentials (rat, pigmented strain preferred) (OPPTS Harmonized Guideline 870.6855)

These studies may be indicated, for example, to follow up neurotoxic signs seen in other studies, or because of structural similarity of the substance to neurotoxicants that affect these endpoints. These studies may be combined with other toxicity studies.

Conclusion: These endpoints do not appear to be applicable to phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester.

Basis for Conclusion: Although there are no studies addressing these endpoints, there are no reliable data for phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester, and no structure-activity considerations, that indicate a current need for these follow-up studies.

IMMUNOTOXICITY

***Conclusion*:**

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available immunotoxicity data were from a guideline study in mice orally exposed to a commercial mixture (Fyrolflex RDP) containing unreported amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl) oxy]phenyl] phenyl ester as a minor component. (Sherwood et al., 2000). The immunotoxicity of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from this study.

$ Immunotoxicity (OPPTS Harmonized Guideline 870.7800)

No adverse effects on survival, body weight, organs related to immune function (thymus and spleen), or results of a battery of immune function tests were observed in mice exposed by oral gavage to undiluted Fyrolflex RDP at doses as high as 5000 mg/kg/day for 28 days (Sherwood et al., 2000).

GENOTOXICITY

Conclusion:

The existing data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The only available genotoxicity data were from guideline studies on commercial mixtures (CR-733-S; Fyrolflex RDP) containing unreported amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester as a minor component. Undefined mixtures elicited negative results in guideline studies for gene mutation in bacteria, and for chromosomal

aberration in vitro and in vivo. The genotoxicity of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these studies.

Gene Mutation in Vitro:

- **Bacterial Reverse Mutation test (OPPTS Harmonized Guideline 870.5100; OECD Guideline 471)**

CR-733-S did not increase the mutation frequency in *Salmonella typhimurium* or *Escherichia coli* at concentrations as high as 5 mg/plate with or without metabolic activation (Covance Labs., 1998); strains used in these studies were not reported in the secondary source (Akzo Nobel, 2001). With or without metabolic activation, Fyrolflex RDP, at concentrations as high as 5 mg/plate, was not mutagenic in *S. typhimurium* strains TA98, TA100, TA1537 or TA1545 (RCC Notox BV, 1988a).

$ **In vitro Mammalian Cell Gene Mutation Test (OPPTS Harmonized Guideline 870.5300; OECD Guideline 476)**

No study of this type was located.

$ **Mitotic Gene Conversion in Saccharomyces cerevisiae (OPPTS Harmonized Guideline 870.5575)**

No study of this type was located.

Gene Mutation in Vivo

No study of this type was located.

Chromosomal Aberrations in Vitro

$ **In vitro Chromosome Aberration Test (OPPTS Harmonized Guideline 870.5375)**

No increase in the incidence of chromosomal aberrations was observed in human peripheral lymphocytes cultured with or without metabolic activation in the presence of CR 733-S (phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester content unknown) at concentrations as high as 0.625 mg/mL (RC Notox BV, 1989g).

Chromosomal Aberrations in Vivo

$ **Mammalian Erythrocyte Micronucleus Test (OPPTS Harmonized Guideline 870.5395; OECD Guideline 474)**

No increase in the incidence of erythrocyte micronuclei was observed in mice given 5000 mg/kg CR-733-S (phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester content unknown) by oral gavage (RCC Notox BV, 1988b).

DNA Damage and Repair

No study of this type was located.

Ecotoxicity

Acute Toxicity to Aquatic Organisms

Conclusion:

The currently available data are not adequate to satisfy the acute toxicity endpoints for fish, aquatic invertebrates, or algae.

Basis for Conclusion:

No pertinent acute toxicity studies with fish, aquatic invertebrates, or algae for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester were located that addressed the endpoints in the guidelines listed below.

- **Acute Toxicity to Freshwater and Marine Fish (OPPTS Harmonized Guideline 850.1075; OECD Guideline 203)**

Experimental fish LD_{50} values of 12.4 mg/L (Akzo Noble, 2001; Great Lakes 2003) and >10,000 mg/L (Bayer, 2002) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the acute toxicity values for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these results. In addition, the experimental LD_{50} values are all much greater than the estimated water solubility for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester, suggesting no effect at saturation.

- **Acute Toxicity to Freshwater Invertebrates (OPPTS Harmonized Guideline 850.1010; OECD Guideline 202)**

Experimental daphnia magna EC_{50} values of 0.76 mg/L (Akzo Noble, 2001) and 178 mg/L (Bayer 2002) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the acute toxicity values for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these results. In addition, the experimental EC_{50} values are all much greater than the estimated water solubility for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester, suggesting no effect at saturation.

- **Acute Toxicity to Marine/Estuarine Invertebrates (OPPTS Harmonized Guideline 850.1035)**
- **Algal Toxicity (OPPTS Harmonized Guideline 850.5400; OECD Guideline 201)**

Experimental algal EC_{50} values of 48.6 mg/L (Akzo Noble, 2001; Great Lakes, 2003) and >10,000 mg/L (Bayer, 2002) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the acute toxicity values for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these results. In addition, the experimental EC_{50} values are all much greater than the estimated water solubility for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester, suggesting no effect at saturation.

Chronic Toxicity to Aquatic Organisms

Conclusion:

The currently available data are not adequate to satisfy the chronic toxicity endpoints for fish or aquatic invertebrates.

Basis for Conclusion:

No pertinent chronic toxicity studies with fish or aquatic invertebrates were located that addressed the endpoints in the guidelines listed below.

- **Chronic Toxicity to Freshwater and Marine Fish (OPPTS Harmonized Guideline 850.1400; OECD Guideline 210)**
- **Chronic Toxicity to Freshwater Invertebrates (OPPTS Harmonized Guideline 850.1300; OECD Guideline 211)**
- **Chronic Toxicity to Marine/Estuarine Invertebrates (OPPTS Harmonized Guideline 850.1350)**

Acute and Subchronic Toxicity to Terrestrial Organisms

Conclusion:

The currently available data are not adequate to satisfy the acute or subchronic toxicity endpoints for terrestrial organisms.

Basis for Conclusion:

No pertinent acute oral, acute dietary, or reproductive toxicity studies with birds and no subchronic toxicity studies with earthworms were located that addressed the endpoints in the guidelines listed below.

- **Acute Oral Toxicity in Birds (OPPTS Harmonized Guideline 850.2100)**
- **Acute Dietary Toxicity in Birds (OPPTS Harmonized Guideline 850.2200; OECD Guideline 205)**
- **Reproductive Toxicity in Birds (OPPTS Harmonized Guideline 850.2300; OECD Guideline 206)**
- **Earthworm Subchronic Toxicity (OPPTS Harmonized Guideline 850.6200; OECD Guideline 207)**

Physical/Chemical Properties

Phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester

CAS	98165-92-5
MF	$C_{42}H_{33}O_{12}P_3$
MW	822.64
SMILES	c1ccccc1OP(Oc2ccccc2)(=O)Oc3cccc(c3)OP(=O)(Oc4ccccc4)Oc5cccc(c5)OP(=O)(Oc6ccccc6)Oc7ccccc7

Water Solubility (mg/L):

Conclusion:

The currently available data are not adequate to satisfy the water solubility endpoint.

Basis for Conclusion:

Experimental data for the water solubility of pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester are not reported in publicly available literature. Experimental water solubility values of <10 mg/L (Akzo Noble, 2001) and 500 mg/L (Chang Chun, no date) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the water solubility values for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these results.

Log K_{ow}:

Conclusion:

The currently available data are not adequate to satisfy the log K_{ow} endpoint.

Basis for Conclusion:

Experimental data for the log K_{ow} of pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester are not reported in publicly available literature. Experimental log K_{ow} values of 4.93 (Wildlife International Ltd., 2003) and 3.9-4.8 (Washington State DOH, 2005) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified in the experimental study details and, therefore, the log K_{ow} values for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these results.

Oxidation/Reduction:

Conclusion:

The currently available data are not adequate to satisfy the oxidation/reduction endpoint.

Basis for Conclusion:

No data are available for the oxidation/reduction endpoint.

Melting Point:

Conclusion:

The currently available data are not adequate to satisfy the melting point endpoint.

Basis for Conclusion:

Experimental data for the melting point of pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester are not reported in publicly available literature. Experimental melting point values of -12 °C (Akzo Noble, 1998; Bayer, 2002; Kirk-Othmer, 2005), -13 °C (Great Lakes, 2003) and -16.7 °C (Akzo Noble, 1998) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the melting point values for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these results.

Boiling Point:

Conclusion:

The currently available data are not adequate to satisfy the boiling point endpoint.

Basis for Conclusion:

Experimental data for the boiling point of pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester are not reported in publicly available literature. Experimental boiling point values of 300 °C (UBA, 2001a, 2003), >300 °C (Akzo Noble, 1998, Bayer, 2002; UBA, 2001b) and 38 °C at 138 Pa (UBA, 2001a, 2001b, 2003), as well as experimental decomposition temperatures of >300 °C (Great Lakes, 2003; UBA, 2001b) and >400 °C (Bayer, 2002) have been reported for commercial mixtures of phosphoric trichloride,

polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the boiling point values for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these results.

Vapor Pressure (torr):

Conclusion:

The currently available data are not adequate to satisfy the vapor pressure endpoint.

Basis for Conclusion:

Experimental data for the vapor pressure of pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester are not reported in publicly available literature. Experimental vapor pressure values of <0.075 torr at 38 °C (Akzo Noble, 2001) and 0.007 torr at 38 °C (UBA, 2001a, 2001b, 2003) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the vapor pressure values for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these results.

Odor:

Conclusion:

The currently available data are not adequate to satisfy the odor endpoint.

Basis for Conclusion:

No data are available for the odor endpoint.

Oxidation/Reduction Chemical Incompatibility:

Conclusion:

The currently available data are not adequate to satisfy the oxidation/reduction chemical incompatibility endpoint.

Basis for Conclusion:

No data is available for the oxidation/reduction chemical incompatibility endpoint.

Flammability:

Conclusion:

The currently available data are not adequate to satisfy the flammability endpoint.

Basis for Conclusion:

No data are available for the flammability endpoint.

Flash Point:

Conclusion:

The currently available data are not adequate to satisfy the flash point endpoint.

Basis for Conclusion:

Experimental data for the flash point of pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester are not reported in publicly available literature. Experimental flash point values of >240 °C (Chang Chun, no date) and 302 °C (Bayer, 2002) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the flash point values for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these results.

Explodability:

Conclusion:

The currently available data are not adequate to satisfy the explodability endpoint.

Basis for Conclusion:

No data are available for the explodability endpoint.

Corrosion Characteristics:

Conclusion:

The currently available data are not adequate to satisfy the corrosion characteristics endpoint.

Basis for Conclusion:

No data are available for the corrosion characteristics endpoint.

pH:

Conclusion:
The currently available data are not adequate to satisfy the pH endpoint.

Basis for Conclusion:

No data are available for the pH endpoint.

UV/VIS Absorption:

Conclusion:

The currently available data are not adequate to satisfy the UV/Vis absorption endpoint.

Basis for Conclusion:

No data are available for the UV/Vis absorption endpoint.

Viscosity:

Conclusion:

The currently available data are not adequate to satisfy the viscosity endpoint.

Basis for Conclusion:

Experimental data for the viscosity of pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester are not reported in publicly available literature. Experimental viscosity values of 240 mPas (Akzo Nobel, 1998), 600 mPas (Akzo Noble, 1998), 500-700 mPas (Bayer, 2002) and 400-800 mPas (Great Lakes, 2003) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the viscosity values for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these results.

Density/Relative Density/Bulk Density:

Conclusion:

The currently available data are not adequate to satisfy the density endpoint.

Basis for Conclusion:

Experimental data for the density of pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester are not reported in publicly available literature. Experimental density values ranging from 1.29 g/cc to 1.32 g/cc (Bayer, 2002); Chang Chun, no date; Great Lakes, 2003) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the density values for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these results.

Dissociation Constant in Water:

Conclusion:

The currently available data are not adequate to satisfy the dissociation constant in water endpoint.

Basis for Conclusion:

No data are available for the dissociation constant in water endpoint.

Henry's Law Constant:

Conclusion:

The currently available data are not adequate to satisfy the Henry's law constant endpoint.

Basis for Conclusion:

No data are available for the Henry's law constant endpoint.

Environmental Fate

Bioconcentration

Fish:

Conclusion:

The currently available data are not adequate to satisfy the fish bioconcentration endpoint.

Basis for Conclusion:

No data are available for the fish bioconcentration endpoint.

Daphnids:

Conclusion:

The currently available data are not adequate to satisfy the daphnid bioconcentration endpoint.

Basis for Conclusion:

No data are available for the daphnid bioconcentration endpoint.

Green Algae:

Conclusion:

The currently available data are not adequate to satisfy the green algae bioconcentration endpoint.

Basis for Conclusion:

No data are available for the green algae bioconcentration endpoint.

Oysters:

Conclusion:

The currently available data are not adequate to satisfy the oysters bioconcentration endpoint.

Basis for Conclusion:

No data are available for the oysters bioconcentration endpoint.

Earthworms:

Conclusion:

The currently available data are not adequate to satisfy the earthworm bioconcentration endpoint.

Basis for Conclusion:

No data are available for the earthworm bioconcentration endpoint.

Fish Metabolism:

Conclusion:

The currently available data are not adequate to satisfy the fish metabolism endpoint.

Basis for Conclusion:

No data are available for the fish metabolism endpoint.

Degradation

Photolysis in the Atmosphere:

Conclusion:

The currently available data are not adequate to satisfy the photolysis in the atmosphere endpoint.

Basis for Conclusion:

No data are available for the photolysis in the atmosphere endpoint.

Photolysis in Water:

Conclusion:

The currently available data are not adequate to satisfy the photolysis in water endpoint.

Basis for Conclusion:

No data are available for the photolysis in water endpoint.

Photolysis in Soil:

Conclusion:

The currently available data are not adequate to satisfy the photolysis in soil endpoint.

Basis for Conclusion:

No data are available for the photolysis in soil endpoint.

Aerobic Biodegradation:

Conclusion:

The currently available data are not adequate to satisfy the aerobic biodegradation endpoint.

Basis for Conclusion:

Experimental data for the aerobic biodegradation of pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester are not reported in publicly available literature. Experimental aerobic biodegradation values of 37% in 28 days and 66% after 56 days (Akzo Noble, 2001) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the aerobic biodegradation values for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these results.

Anaerobic Biodegradation:

Conclusion:

The currently available data are not adequate to satisfy the anaerobic biodegradation endpoint.

Basis for Conclusion:

No data are available for the anaerobic biodegradation endpoint.

Porous Pot Test:

Conclusion:

The currently available data are not adequate to satisfy the porous pot test endpoint.

Basis for Conclusion:

No data are available for the porous pot test endpoint.

Pyrolysis:

Conclusion:

The currently available data are not adequate to satisfy the pyrolysis endpoint.

Basis for Conclusion:

No data are available for the pyrolysis endpoint.

Hydrolysis as a Function of pH:

Conclusion:

The currently available data are not adequate to satisfy the hydrolysis as a function of pH endpoint.

Basis for Conclusion:

Experimental data for the hydrolysis as a function of pH of pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester are not reported in publicly available literature. Experimental hydrolysis half-life values of 11 days at pH 4, 17 days at pH 7 and 21 days at pH 9 (Akzo Noble, 2001) and of 17 days at pH 7 (European Flame Retardants Association, no date) have been reported for commercial mixtures of phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (125997-21-9) which contain varying amounts of phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester. The percentage of each of the individual components of these mixtures is not specified and, therefore, the hydrolysis values for pure phosphoric acid, bis[3-[(diphenoxyphosphinyl)oxy]phenyl] phenyl ester cannot be determined from these results.

Sediment/Water Biodegradation:

Conclusion:

The currently available data are not adequate to satisfy the sediment/water biodegradation endpoint.

Basis for Conclusion:

No data are available for the sediment/water biodegradation endpoint.

Soil Biodegradation with Product Identification:

Conclusion:

The currently available data are not adequate to satisfy the soil biodegradation with product identification endpoint.

Basis for Conclusion:

No data are available for the soil biodegradation with product identification endpoint.

Indirect Photolysis in Water:

Conclusion:

The currently available data are not adequate to satisfy the indirect photolysis in water endpoint.

Basis for Conclusion:

No data are available for the indirect photolysis in water endpoint.

Sediment/Soil Adsorption/Desorption:

Conclusion:

The currently available data are not adequate to satisfy the sediment/soil adsorption/desorption endpoint.

Basis for Conclusion:

No data are available for the sediment/soil adsorption/desorption endpoint.

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Flame Retardant Alternative WS-5:
Triphenyl Phosphate

Hazard Review

Triphenyl Phosphate:
Existing Data Summary Table – Human Health Endpoints

T= Endpoint characterized by existing data * = Data available but not adequate	Ψ = Endpoint not applicable

Acute Toxicity	
Oral	T
Dermal	T
Inhalation	*
Eye irritation	T
Dermal irritation	T
Skin sensitization	*
Subchronic Toxicity	
28-Day oral	*
90-Day oral	*
Combined repeated dose with reproduction/ developmental toxicity screen	
21/28-Day dermal	*
90-Day dermal	
90-Day inhalation	
Reproductive Toxicity	
Reproduction/ developmental toxicity screen	*
Combined repeated dose with reproduction/ developmental toxicity screen	
Reproduction and fertility effects	

Developmental Toxicity	T
Reproduction/ developmental toxicity screen	
Combined repeated dose with reproduction/ developmental toxicity screen	
Prenatal developmental	T
Chronic Toxicity	
Chronic toxicity (two species)	
Combined chronic toxicity/ carcinogenicity	
Carcinogenicity	
Carcinogenicity (rat and mouse)	
Combined chronic toxicity/ carcinogenicity	

Neurotoxicity	
Acute and 28-day delayed neurotoxicity of organophosphorus substances (hen)	T
Neurotoxicity screening battery (adult)	T
Developmental neurotoxicity	
Additional neurotoxicity studies	Ψ
Immunotoxicity	T
Immunotoxicity	T
Genotoxicity	
Gene mutation in vitro	T
Gene mutation in vivo	
Chromosomal aberrations in vitro	
Chromosomal aberrations in vivo	
DNA damage and repair	
Other	T

Triphenyl Phosphate:
Existing Data Summary Table – Properties, Fate, and Ecotoxicity

T= Endpoint characterized by existing data * = Data available but not adequate	Ψ = Endpoint not applicable

P/Chem Properties	
Water solubility	T
Octanol/water partition coefficient	T
Oxidation/reduction	
Melting point	T
Boiling point	T
Vapor pressure	T
Odor	T
Oxidation/reduction chemical incompatibility	
Flammability	T
Explodability	
Corrosion characteristics	
pH	
UV/visible absorption	T
Viscosity	
Density/relative density/bulk density	T
Dissociation constant in water	Ψ
Henry's Law constant	T

Environmental Fate	
Bioconcentration	
Fish	T
Daphnids	
Green algae	
Oysters	
Earthworms	
Metabolism in fish	*
Degradation and Transport	
Photolysis, atmosphere	
Photolysis, water	T
Photolysis in soil	
Aerobic biodegradation	T
Anaerobic biodegradation	
Porous pot test	
Pyrolysis	*
Hydrolysis as a function of pH	T
Sediment/water biodegradation	T
Soil biodegradation w/ product identification	T
Indirect photolysis in water	
Sediment/soil adsorption/desorption	T
Ecotoxicity	
Aquatic Toxicity	
Fish acute LC50	T
Daphnia acute EC50	T
Mysid shrimp acute LC50	*
Green algae EC50, NOAEC, LOAEC	T

Fish chronic NOAEL, LOAEC	*
Daphnia chronic NOAEC, LOAEC	
Mysid shrimp chronic NOAEC, LOAEC	
Sediment organisms	*
Terrestrial Organism Toxicity	
Bird LD50 (two species)	
Bird LC50 (two species)	
Bird reproduction	
Earthworm subchronic EC50, LC50, NOAEC, LOAEC	

Chemical Identity

Triphenyl phosphate

CAS	115-86-6
MF	$C_{18}H_{15}O_4P$
MW	326.29
SMILES	c1ccccc1OP(=O)(Oc2ccccc2)Oc3ccccc3

Human Health Endpoints

The OPPTS Harmonized Test Guidelines are the preferred criteria for study adequacy, but the corresponding OECD Guidelines are also considered. The available studies generally predate these guidelines, as well as Good Laboratory Practice guidelines, although some studies were conducted in a manner similar to guideline specifications. For some endpoints, several studies of variable quality are available, allowing the weight of evidence to characterize the endpoint despite inadequacies of the individual studies. Studies that were published in a foreign language, or that were not readily available, and that were not critical to the hazard assessment were not retrieved.

The relevance of health effects studies in laboratory animals to humans needs to be considered in the context of anticipated human exposure patterns. For example, adverse effect levels measured following bolus exposure in oral gavage studies in animals may not directly pertain to human exposures from drinking water in which intakes occur over a longer time period during a day. The more gradual intakes are less likely to overwhelm detoxification processes than bolus delivery.

ACUTE TOXICITY

Acute Oral Toxicity (OPPTS Harmonized Guideline 870.1100; OECD Guidelines 425, 420, 423, 401).

Conclusion:

The available acute oral toxicity data were judged adequate to meet the endpoint.

Basis for Conclusion:

Several acute oral lethality studies were available in a variety of species: rats, mice, rabbits, guinea pigs, and hens. These studies were from the older (pre 1980) literature, and do not fully conform to OPPTS or OECD guidelines, but together may be adequate to support the evaluation of acute oral toxicity. The toxic potency of TPP tended to be somewhat lower when it was

administered in aqueous vehicle (usually as a suspension) than when administered in oil. Deaths generally did not occur following administration in aqueous vehicle ([LD50 >5,000-20,000 mg/kg), and were seen at relatively high doses (LD50 = 10,800 mg/kg) from administration in oil. Two of the better studies in the preferred species (rat), one using an aqueous vehicle and the other using an oil vehicle, and one each in mice and rabbits using an aqueous vehicle, are summarized below as the critical studies.

Critical Studies:

Type: Acute oral limit test
Species, strain, sex, number: Rat, Wistar, 5 male and 5 female
Dose: 20,000 mg/kg
Purity: Not reported, Monsanto commercial TPP
Vehicle: Water: 25% aqueous "solution"
Method: Similar to limit test, but higher dose; 24-hour fasting period prior to dosing; 14-day post-dosing observation period; observations limited to mortality and necropsy
Results: No deaths, therefore LD50 >20,000 mg/kg. Necropsy revealed sporadic visceral hemorrhages.
Reference: Food and Drug Research Labs, 1976

Type: Acute oral LD50
Species, strain, sex, number: Rat, Sprague-Dawley, male and female, number not specified
Dose: Up to 15,800 mg/kg
Purity: GC-verified, but not specifically reported
Vehicle: Corn oil
Observation period: 14 days post dosing
Method: LD50 calculated according to DeBeer (1945); not specified whether fed or fasted at time of dosing; 14-day post-exposure observation period; mortality only
Results: LD50 = 10,800 mg/kg; actual mortality data not reported
Reference: Johannsen et al., 1977

Type: Acute oral limit test
Species, strain, sex, number: Mouse, strain not specified, male and female, 5 total/dose
Doses: 2,500 and 5,000 mg/kg
Purity: Not specified
Vehicle: Emulsion in aqueous gum acacia
Method: Similar to limit test; not specified whether fed or fasted at time of dosing; 8-day observation period; observations limited to mortality and overt signs
Results: No deaths at either dose; therefore, LD50 >5,000 mg/kg; slight stupor
Reference: Ciba-Geigy Ltd., 1954

Type: Acute oral limit test

Species, strain, sex, number: Rabbit**,** strain and sex not specified, 1/dose
Purity: Technical grade TPP
Doses: 3,000 and 5,000 mg/kg
Vehicle: Suspended in aqueous gum acacia
Method: Preliminary limit test, observation was for "several days", observations limited to clinical signs and mortality
Results: Neither rabbit died, indicating LD >5,000 mg/kg; both had diarrhea
Reference: Dow Biochemical Research, 1934

Additional Studies and Information:

Other studies that were of lesser quality or were reported in less detail are generally consistent with the above studies (Houghton EF & Company, no date; Kettering Lab, 1945; Smith et al., 1932; Sutton et al., 1960).

Specific organ toxicity was generally not observed in the studies that include gross pathological examinations. Some signs possibly indicative of neurotoxicity (lassitude incoordination, tremors, or weakness) were observed in a few studies (Ciba-Geigy Ltd. 1954; Kettering Lab, 1945; Smith et al., 1932). It has been suggested that at the very high doses employed in these acute toxicity studies, even small amounts of impurities could be responsible for the apparent neurotoxicity, which has not been seen with purified TPP (see section on neurological effects), or that the signs may have been secondary to other effects.

Acute Dermal Toxicity (OPPTS Harmonized Guideline 870.1200; OECD Guideline 402)

Conclusion:

The available acute dermal toxicity data were judged adequate to meet the endpoint.

***Basis for Conclusion*:**

The available studies predate the preferred study guidelines, and lack details including purity and discussion of necropsy results, but together indicate a low order of toxicity (LD50>7,900-10,000 mg/kg), consistent with the acute oral studies.

Type: Acute dermal toxicity
Species, strain, sex, number: Rabbit, albino, sex not specified, 10
Dose: 10,000 mg/kg
Purity: No data, commercial product provided by Monsanto, white flakes
Vehicle: Not reported, but the concurrent acute oral study used water
Method: U.S. Federal Hazardous Substances Act Regulations study guideline16 CFR 1500.40; 5 rabbits tested with intact skin and 5 with abraded skin; 14-day observation period

Results: Mortality after 14 days 0/5 intact, 0/5 abraded. Therefore, LD50 >10,000 mg/kg.
Reference: Food and Drug Research Labs, 1976

Type: Acute dermal toxicity
Species, strain, sex, number: Rabbit, New Zealand albino, sex and number not specified
Dose: Highest dose = 7,900 mg/kg
Purity: No data, prepared from pure phenol
Vehicle: None ("undiluted")
Method: Intact skin, occlusive dressing, test material washed off after 24 hours, 14-day observation period. Necropsy.
Results: No deaths; therefore, LD50 >7,900 mg/kg; necropsy results not discussed.
Reference: Johanssen et al., 1977

Acute Inhalation Toxicity (OPPTS Harmonized Guideline 870.1300 (OECD Guideline 403)

Conclusion:

The available acute inhalation toxicity data were judged inadcquate to meet the endpoint unless data regarding particle size in the TPP powder study are provided.

Basis for Conclusion:

The available studies on TPP predate the preferred guidelines, but the study using TPP powder (Food and Drug Research Labs, 1976) was reported to be conducted according to a guideline that was relevant at the time. The duration was shorter than currently recommended and the concentration was much higher, but no signs of toxicity and no deaths were observed. Analysis of particle size, however, was not mentioned, so it is not known whether the size was respirable. Necropsies apparently were not performed. The other available study, on TPP vapor (Sutton et al., 1960), was conducted at an exposure level lower than recommended for a limit test, the observation period was inadequate, and it appears that the chamber was a closed chamber, which is not according to guideline.

Type: Acute inhalation toxicity
Species, strain, sex, number: Rat, Wistar, 5 males and 5 females
Doses: 200 mg/L (nominal); administered as a powder; particle size not reported
Purity: No data, commercial product provided by Monsanto, white flakes
Vehicle: None
Duration: 1 hour
Method: 16 CFR 1500.3; 300 mL chamber with air flow of 5 L/minute. Observation period = 14 days. Observed daily for signs of toxicity and for mortality.
Results: Mortality after 14 days 0/5 males, 0/5 females; no overt signs of toxicity
Reference: Food and Drug Research Labs, 1976

Type: Acute inhalation toxicity
Species, strain, sex, number: Mouse, Carworth Farms CF 1, male
Doses, duration, number: 363 mg/m^3 (6 hours exposure, 5 mice) and 757 mg/m^3 (2 and 4 hours exposure, 7 mice/duration)
Purity: Practical Grade Eastman
Vehicle: None
Method: The mice were exposed to TPP vapor in a battery jar following generation of the vapor by flowing preheated air through molten TPP at 175-180EC. Observation period = 24 hours. The mice were observed for signs of cholinergic toxicity and blood cholinesterase was measured at termination.
Results: No overt signs of toxicity; cholinesterase determinations not considered valid because controls did not appear to have been sham exposed.
Reference: Sutton et al., 1960

Acute Eye Irritation (OPPTS Harmonized Guideline 870.2400; OECD Guideline 405)

Conclusion:

The available eye irritation data were judge adequate to meet the endpoint.

Basis for Conclusion:

Two reasonably adequate studies report similar results in rabbits: mild reversible irritation primarily of the conjunctiva. The studies are summarized below.

Type: Acute eye irritation
Species, strain, sex, number: Rabbit, albino, sex not specified; 9
Doses: 100 mg
Purity: No data, commercial product provided by Monsanto, white flakes
Vehicle: Not reported
Method: Patterned after U.S. Federal Hazardous Substances Act Regulations study guideline 16 CFR 1500.42, except 6 rabbits–eyes not washed after instillation of TPP, 3 rabbits–eyes washed 4 seconds following instillation of TPP; eyes examined at 24, 48, and 72 hours, and 7 days after instillation of TPP.
Results: Mild conjunctival effects (slight redness 6/6, slight discharge 4/6) at 24 hours in the eyes that were not washed out, which cleared by 72 hours; no effects in eyes that had been washed out (incidence 0/3).
Reference: Food and Drug Research Labs, 1976

Type: Acute eye irritation
Species, strain, sex, number: Rabbit, New Zealand, 3 males and 3 females

Doses: 100 mg
Purity: No data, commercial product provided by Monsanto, white flakes
Vehicle: None
Method: Patterned after U.S. Federal Hazardous Substances Labeling Act Section 191.12 (February 1965). Eyes of 3 (of the 6) rabbits were washed out 30 seconds following instillation of TPP; eyes examined at 1, 24, 48, and 72 hours and 6 days after TPP instillation.
Results: Mild conjunctival effects (slight redness 6/6) at 24 hours in all exposed eyes, which cleared in all but 1 (unwashed) eye by 72 hours; and in that eye by 6 days. Slight corneal opacity was seen in one unwashed eye at 24 hours, which cleared by 48 hours.
Reference: Ciba-Geigy Pharmaceuticals Division, 1983a

Acute Dermal Irritation (OPPTS Harmonized Guideline 870.2500; OECD Guideline 404)

Conclusions:

The available dermal irritation data were judged adequate to meet the endpoint.

Basis for Conclusions:

Two reasonably adequate studies, patterned after guidelines in effect at the time, provide similar results, indicating that TPP was not a skin irritant in rabbits. Additional studies provide support. The studies are summarized below.

Critical Studies:

Type: Acute dermal irritation
Species, strain, sex, number: Rabbit, albino, sex not specified, 6
Doses: 500 mg
Purity: No data, commercial product provided by Monsanto, white flakes
Vehicle: Not reported, but acute oral study used water
Method: Patterned after U.S. Federal Hazardous Substances Act Regulations study guideline 16 CFR 1500.41; shaved back, each rabbit tested on intact and abraded skin, semiocclusive dressing removed after 24 hours, observations at 24 and 72 hours.
Results: No erythema or edema on intact or abraded skin in any of the 6 rabbits.
Reference: Food and Drug Research Labs, 1976

Type: Acute dermal irritation
Species, strain, sex, number: Rabbit, New Zealand, 3 males and 3 females
Doses: 1.0 mL of suspension of 10,000 mg/20 mL = 500 mg
Purity: No data, white flakes
Vehicle: 50% aqueous solution of polyethylene glycol

Method: U.S. Federal Hazardous Substances Labeling Act Section 191.12 (February 1965); shaved back, each rabbit tested on intact and abraded skin, occlusive dressing removed after 24 hours, observations at 24 and 72 hours.
Results: No erythema or edema on intact or abraded skin in any of the 6 rabbits.
Reference: Ciba-Geigy Pharmaceuticals Division, 1983b

Additional Studies:

Other studies, reported in less detail, also reported no effects in rabbits from dermal exposure on intact skin to the dry powdered TPP, and only slight dryness during repeated application as a saturated solution in ethanol (13 times in 16 days) (Dow Biochemical Research, 1933).

Skin Sensitization (OPPTS Harmonized Guideline 870.2600; OECD Guideline 429)

Conclusion:

The available skin sensitization data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No experimental studies of skin sensitization in animals were located in the published literature. A few human cases of TPP allergic dermatitis have been reported. An example is a case of allergy to TPP from cellulose acetate eyeglass frames that contained TPP as an additive (Carlsen et al., 1986). Patch testing of dermatological patients, however, has not generally implicated this chemical as a sensitizer. For example, of 343 patients tested because of suspected sensitivity to plastics and glues components, none reacted to TPP (Tarvainen, 1995). In a study of 23,192 patents with eczema who were patch tested with cellulose acetate film containing 7-10% TPP and 4-5 % phthalic acid, positive reactions were observed in only 15 (0.065%) (Hjorth 1964).

SUBCHRONIC TOXICITY

Subchronic Oral Toxicity (28-day, 90-day, or combined with reproductive/developmental)

Conclusion:

The available subchronic oral toxicity data were judge inadequate to meet the endpoint, but an existing unpublished Food and Drug Administration (FDA) study, if provided, could address this data gap.

Basis for Conclusion:

A single 35-day study in rats (Sutton et al., 1960) provides limited relevant information. The study was not adequate to characterize this endpoint because of the small number of rats in each dose group, testing of only one sex, lack of clinical chemistry and histopathology data, and lack of detailed reporting. A set of concurrent approximately 120-day studies performed by FDA investigated general toxicity, reproductive and developmental toxicity, neurotoxicity, and immunotoxicity (Hinton et al., 1987, 1996; Sobotka et al., 1986; Welsh et al., 1987). The general toxicity study, however, was not published, and the associated studies do not report adequate information on the general toxicity of this chemical.

$ Repeated Dose 28-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3050; OECD Guideline 407)

The only relevant available study is a 35-day repeated oral study that does not satisfy the guideline. A summary of the study is as follows:

Type: 35-Day repeated oral
Species, strain, sex, number: Rat, Holtzman, male, 5/dose
Doses: 0, 0.1, and 0.5% in the diet (the 0.1% group received 5% for the first 3 days, but refused to eat, and therefore was switched to a lower dietary concentration)
Purity: Practical Grade Eastman Organic, purity not specified
Vehicle: None; added to diet
Exposure period, frequency: 35 days, daily
Post Exposure Period: 2 weeks
Method: Two rats/group killed at end of 35 days; 3 rats/group observed for 2 week recovery period; body weight, hematology (hemoglobin, cell volume, red and white cell count, and differential), necropsy with organ weights.
Results: Slight depression in body weight gain in high dose group at day 35, but not after 2-week recovery period. Slight but statistically significant increase (Student's t test) in mean relative liver weight in high dose group–not specified whether all 5 rats/group were included in organ weight determinations. No gross abnormalities seen at necropsy. No statistically significant differences in hematological values.
Reference: Sutton et al., 1960

$ 90-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3100; OECD Guideline 408)

The only ∃90 day subchronic studies of TPP toxicity were specialized studies of reproductive, developmental, neurological, and immunological endpoints in the rat conducted by the FDA (Hinton et al., 1987; Sobotka et al., 1986; Welsh et al., 1987). These studies provide only limited information on other systemic toxicities, and therefore do not satisfy the guideline.

- $ In the reproductive and developmental toxicity study in the rat, males and females were fed TPP at dietary levels up to 1% for 91 days prior to mating, continuing through mating, and the females were continued on the diet until day 20 of gestation. This study reported no differences in behavior or gross pathology of the treated dams, a slight but significant decrease on day 0 of gestation in the body weight of the dams fed the 1% diets (690 mg/kg/day), a slight but significant increase in food consumption primarily at 0.5 and 0.75% in the diet(not dose-related), and a non-significant decrease in body weight gain (minus the gravid uterus) at day 20 of gestation in dams fed ∃0.5% (341 mg/kg/day) (Welsh et al., 1987).
- $ The neurological study, in which male rats were fed up to 1% TPP in the diet for 4 months, provided no evidence of neurobehavioral effects, but also noted a decrease in body weight gain. The NOAEL and LOAEL for this effect were 0.25% in the diet (161 mg/kg/day) and 0.50% in the diet (345 mg/kg/day) (Sobotka et al., 1986).
- $ In the immunotoxicity study, in which male and female rats were fed up to 1% TPP in the diet for 4 months, the only effects seen were a decrease in body weight gain at 1.0% (approximately 700 mg/kg/day) in the diet, and non-dose related increases in the relative percentages of ∀-globulins in treated females and ∃-globulins in treated males, which were interpreted as a possible sign of liver activity of uncertain toxicological significance (Hinton et al., 1987). Because of the lack of dose-response, these findings may not be indicative of a chemical effect. The NOAEL and LOAEL for decreased body weight gain were 0.75% in the diet (517 mg/kg/day) and 1.0% in the diet (700 mg/kg/day).

Details of these studies are provided in the appropriate sections. These studies are not adequate to fulfill the requirements of the 90-day subchronic oral toxicity guideline.

An associated, concurrent FDA subchronic toxicity study, mentioned in the other FDA reports (Hinton et al., 1987, 1996; Sobotka et al., 1986; Welsh et al., 1987), has not been published. The study has been requested for review.

- $ **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**

No studies of this type were located.

Subchronic Dermal Toxicity (21/28-day or 90-day)

Conclusion:

The available subchronic dermal toxicity data are judged inadequate to meet the endpoint unless further information is provided for the available 21-day study.

Basis for Conclusion:

The only study available for this endpoint, a 21-day dermal toxicity study, has a design similar to that of the OPPTS guideline, but the reporting of the study is deficient. Only the text portion of the results was available, but the tables summarizing the data were omitted, as were data regarding the outcome of tests of purity of the TPP. Because it is the only relevant study, more detailed reporting of information from this study is needed if it is to be used to satisfy the endpoint. The study is summarized below.

$ 21/28-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3200 (OECD Guideline 410)

Type: 21-Day dermal toxicity
Species, strain, sex, number: Rabbit, New Zealand white, 10 males and 10 females/dose
Doses: 0 (vehicle control), 100, and 1,000 mg/kg body weight
Purity: Determined at start and end of test but results not reported
Vehicle: Absolute ethanol
Exposure period, frequency: 21-23 days, 5 days/week
Post Exposure Period: none
Method: Similar to 870.3200 but functional observational battery omitted, number of tissues/organs examined histopathologically was not as extensive, and histopathological examinations were performed on all control and high dose rabbits and "as required" on low dose rabbits. The skin of 5 males and 5 females in each dose group was abraded twice a week; the skin of the other 5 males and 5 females in each group was not. No dressing was used after application of the vehicle or test substance, but collars were used to prevent contact with the material, and the excess was removed after 6 hours.
Results: No treatment-related changes were seen in clinical signs, mortality, body weight, hematology, gross or histopathology, or routine clinical chemistry. Low-dose females had decreased mean thyroid/body weight ratio and increased mean kidney weight. Dose-related depressions in serum, erythrocyte, and brain cholinesterase were observed. The tables summarizing the actual data were omitted from the report.
Reference: Bio/Dynamics, Inc., 1970

$ 90-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3250; OECD Guideline 411)

No studies of this type were located.

Subchronic Inhalation Toxicity: 90-Day Inhalation Toxicity (OPPTS Harmonized Guideline 870.3465; OECD Guideline 413)

Conclusion:

The available subchronic inhalation toxicity data for nonrodents were judged inadequate to meet the endpoint.

Basis for Conclusion:

No repeated-exposure inhalation toxicity studies were located.

REPRODUCTIVE TOXICITY

Conclusion:

The available reproductive toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

A study of reproduction and development in rats exposed for 91 days prior to mating, and continuing through mating until day 20 of gestation (Welsh et al., 1987) partially characterizes this endpoint, but is not fully adequate. No other data relevant to this endpoint were located.

$ Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)

A study of reproduction and development in rats exposed for 91 days prior to mating, and continuing through mating until day 20 of gestation (Welsh et al., 1987) partially satisfies the reproductive screening component of this guideline, but is not fully adequate, primarily because it lacks histopathology of male and female reproductive organs. The study is summarized below under Developmental Toxicity. Findings relevant to reproduction were that there were no significant differences in number of corpora lutea, implants, implantation efficiency, viable fetuses, and number of early or late deaths at dietary levels as high as 1.0% TPP (690 mg/kg/day). Because both sexes were treated, and there were no effects on litter size (as measured by number of viable fetuses), the study provides some evidence that fertility is not affected by TPP in the rat.

$ Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)

No studies with this specific design were available.

$ Reproduction and Fertility Effects (OPPTS Harmonized Guideline 870.3800; OECD Guideline 416)

No studies with this specific design (two-generation reproduction) were available.

DEVELOPMENTAL TOXICITY

Conclusion:

The available developmental toxicity data were judged adequate to meet the endpoint.

Basis for Conclusion:

A study of reproduction and development in rats exposed for 91 days prior to mating, and continuing through mating until day 20 of gestation (Welsh et al., 1987) appears to fulfill the requirements of the Prenatal Developmental Toxicity Study guideline, and is adequate to characterize developmental toxicity. Details of this study are as follows:

$ Prenatal Developmental Toxicity Study (OPPTS Harmonized Guideline 870.3700; OECD Guideline 414)

Type: Reproductive screen, prenatal developmental toxicity
Species, strain, sex, number: Rat, Sprague-Dawley, 40 males and 40 females/dose
Purity: Commercial grade, Aldrich, 98% pure
Doses: 0, 0.25, 0.50, 0.75, or 1.00% in the diet (0, 166, 341, 516, and 690 mg/kg/day based on food consumption and body weight of pregnant females)
Exposure duration, frequency: Starting at 4 weeks post weaning, males and females exposed for 91 days prior to mating, continuing through mating and, for the dams, through gestation day 20; daily
Method: Body weight, food consumption, clinical signs, and necropsy of dams; uterine contents at day 20 of gestation; fetal weight, crown-rump length, external, visceral, and skeletal abnormalities; extensive statistical analyses.
Results: The body weights of the females fed the 1.0 % diets were slightly but significantly lower than those of controls on day 0 of gestation. During gestation, the dams that consumed TPP in the diet generally consumed slightly more food than controls; but their body weight gains during gestation and the adjusted body weight gain (excluding gravid uterus) at day 20 were not significantly different from controls. No differences in behavior or gross pathology were reported. Fertility (pregnancy rate) was higher in the treated females than in controls, but control fertility was relatively low. No significant differences between treated and control groups were seen for numbers of corpora lutea, implants, implantation efficiency, viable fetuses, or resorptions (total or early or late deaths). Male and female fetuses from the treated groups

tended to weigh more than control fetuses, but the differences were minimal (<10% increase in fetal weight), not dose-related, and significant ($p<0.05$) only for the males in the 0.50 and 1.00% groups (but not the 0.75% group). Significant, slight increases in visceral variations (moderate hydroureter, enlarged ureter proximal to kidney) were seen in litters of all treated groups, but the increases were not dose-related, and the controls had a relatively high incidence of moderate hydroureter. Given the lack of dose response and uncertain biological significance of the slight fetal changes in this study, the highest dose level (1.0% TPP in the diet, 690 mg/kg/day) may be a NOAEL for fetotoxicity. TPP did not produce teratogenic effects in this study. This study suggests a minimal LOAEL for decreased body weight gain of 1.0% TPP in the diet (690 mg/kg/day) for the dams. Although the highest dose in the study (1.0% in the diet, 690 mg/kg/day) is not as high as a limit dose of 1,000 mg/kg/day, it did produce slight body weight depression in the dams, and in the two associated studies (on neurotoxicity and immunotoxicity), produced more striking depressions in body weight gain in male and female rats at the same dietary level, particularly in the first few weeks on test, and in the absence of a depression in food consumption. A higher dietary level (5%) was tested in a 35-day study in rats and resulted in food refusal (Sutton et al., 1960). Thus testing with dietary levels substantially higher than 1.0% TPP may not be advisable.
Reference: Welsh et al., 1987

$ Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)

No studies with this specific design were available.

$ Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)

A study of reproduction and developmental toxicity is available (Welsh et al., 1987); the developmental toxicity portion of the study is consistent with a full prenatal developmental toxicity study, and was discussed previously under that category.

CHRONIC TOXICITY

Conclusion:

The available chronic toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No relevant studies were located.

$ Chronic Toxicity (OPPTS Harmonized Guideline 870.4100; OECD Guideline 452)

No studies of this type were located.

$ Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)

No studies of this type were located.

CARCINOGENICITY

Conclusion:

The available carcinogenicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

The available study, a strain A mouse pulmonary adenoma study, is not a suitable type of study to characterize the potential carcinogenicity of chemicals for chronic oral exposure. The study is summarized below.

Type: Strain A mouse pulmonary adenoma
Species, strain, sex, number: Mouse, strain A/St, 20 males/dose
Identity: Uncertain—reported as triphenyl phosphate, and also as phosphorous acid, triphenyl ester (which is triphenyl phosphite, a different chemical)
Purity: Not reported, Aldrich, reagent grade
Doses: 0 (vehicle control), 20, 40, and 80 mg/kg
Vehicle: Tricaprylin
Route: Intraperitoneal injection
Exposure duration, frequency: 3 injections/week; for 20 mg/kg–18 injections (6 weeks), for 40 mg/kg–3 injections (1 week), for 80 mg/kg–1 injection (the experimental design was to give 24 injections, but fewer injections were given for the "more toxic chemicals".
Method: 24 weeks after the first injection, the mice were killed and the lungs were examined for surface nodules; a few of the nodules were examined histologically to confirm that they were adenomas; positive controls received urethan; Student t test.
Results: Survival at 24 weeks was 46/50 for controls, 18/20 at 20 mg/kg (18 injections), 3/20 at 40 mg/kg (3 injections), and 12/20 at 80 mg/kg (1 injection). No increase in the number of pulmonary adenomas/mouse was seen.
Reference: Theiss et al., 1977

$ Carcinogenicity (OPPTS Harmonized Guideline 870.4200; OECD Guideline 451)

No studies of this type were located.

$ Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)

No studies of this type were located.

NEUROTOXICITY

Conclusion:

The available neurotoxicity data were judged not fully adequate to meet the endpoint.

Basis for Conclusion:

Some components of this endpoint—delayed neurotoxicity and neurotoxicity screening (in adult animals)—are satisfied by the existing data, but no study of developmental neurotoxicity has been conducted. This endpoint could be addressed in combination with the reproductive toxicity endpoint. TPP gave negative results in several acute oral delayed neurotoxicity studies in the hen as well as a subcutaneous study in the cat, and also in a subchronic oral neurotoxicity screening study in the rat. Further information is provided in the following subsections.

Delayed Neurotoxicity

Conclusions:

The available delayed neurotoxicity data are judged adequate to meet the endpoint.

Basis for Conclusion:

The available acute delayed neurotoxicity studies in the hen and in the cat (another sensitive species), summarized below, give no evidence of acute cholinergic toxicity or of delayed neurotoxicity. These studies, performed prior to the existence of the guidelines, do not entirely conform to the guidelines, and lack detail including, in the hen studies, purity of the TPP sample. Nevertheless, together they indicate a lack of delayed neurotoxicity for TPP. Neurotoxic esterase (NTE) assays were not conducted in these studies. In a separate unpublished study, summarized in a review of structure-activity studies, an NTE assay in brain homogenate following a single oral dose of 700 mg/kg TPP (>99% purity) to the hen (Johnson, 1975) gave negative results. This dose is lower than those used in the critical studies of delayed

neurotoxicity in hens but given the lack of signs and histopathological evidence for delayed neurotoxicity, additional NTE assays do not appear necessary.

Because of the lack of signs or histopathology indicating delayed neurotoxicity in the acute studies, 28-day studies are not required. In addition, structure-activity studies indicate that TPP would not be expected to cause delayed neurotoxicity (Johnson, 1975).

$ Acute and 28-Day Delayed Neurotoxicity of Organophosphorus Substances (OPPTS Harmonized Guideline 870.6100; OECD Guideline 418, 419)

Critical Studies

Type: Delayed neurotoxicity
Species, strain, sex, number: Hen, White Leghorn, 9 for TPP
Purity: Not reported, prepared from pure phenol
Doses: 5,000 mg/kg twice daily; thus, 10,000 mg/kg/day
Vehicle: Corn oil
Route: Gavage
Exposure duration, frequency: Twice a day on days 1-3 and 21-23 of the study (6 days of dosing); interval between doses not reported.
Method: Dosing twice daily for 6 days was needed because of the low toxicity of TPP (no lethality at 5 mg/kg, the largest feasible dose). Hens were fasted for 16 hours before dosing (further explanation not provided). Daily observations for deaths and signs of neurotoxicity were conducted from day 1 through day 42, at which time hens were necropsied. Brain, sciatic nerve, and spinal cord were examined histopathologically. Tricresyl phosphate (mixed o-, m-, p-) was tested concurrently.
Results: For TPP, no overt signs of neurotoxicity and no histopathological effects in the nervous tissues were observed (0/9). Although the hens were weighed at 0, 21, and 42 days, no body weight results were presented. Tricresyl phosphate, a known delayed neurotoxicant, resulted in overt signs and histopathological evidence of delayed neurotoxicity in 6/6. Details of the histopathological data were not provided.
Reference: Johannsen et al., 1977

Type: Delayed neurotoxicity
Species, strain, sex, number: Hen, Rhode Island Red x Light Sussex, 2/dose
Purity: Not reported, white flakes
Doses: 2,000, 3,000, 5,000, 8,000, or 12,500 mg/kg
Vehicle: Arachis oil
Route: Gavage
Exposure duration, frequency: Single dose
Method: Hens were not fasted. Post-dosing observation period was 21 days. Daily observations for deaths and signs of neurotoxicity. Necropsy but not histopathology.

Results: No overt signs of neurotoxicity. Necropsy results not mentioned.
Reference: Ciba-Geigy Pharmaceuticals Division, 1980

Type: Delayed neurotoxicity
Species, strain, sex, number: Hen, Rhode Island Red x Light Sussex, 2
Purity: Not reported, white flakes
Doses: 12,000 mg/kg
Vehicle: Arachis oil
Route: Gavage
Exposure duration, frequency: Single dose
Method: Hens were not fasted. Post-dosing observation period was 21 days. Daily observations for deaths and signs of neurotoxicity. Necropsy but not histopathology.
Results: No overt signs of neurotoxicity, and no abnormalities at necropsy.
Reference: Ciba-Geigy Pharmaceuticals Division, 1981a

Type: Delayed neurotoxicity
Species, strain, sex, number: Cat, not further specified, 5
Purity: Zone-refined triphenyl phosphate, purity 99.99%
Doses, number: 400 mg/kg in propylene glycol (2 cats), 700 mg/kg in corn oil (2 cats), and 1,000 mg/kg in corn oil (1 cat)
Vehicle: Propylene glycol (1 cat), corn oil (2 cats)
Route: Subcutaneous injection
Exposure duration, frequency: Single dose
Method: Post-dosing observation period was 4 months. Daily observations for deaths, general behavior, eating, and drinking. Weighed at intervals. Whole blood, plasma, and erythrocyte cholinesterase determined for cats given 700 mg/kg of TPP and their controls. Complete necropsies on cats given 700 mg/kg. Brain stem and spinal cord examined histopathologically in all cats.
Results: All except one on the lowest dose lost weight (due to cessation of eating); the other on the lowest dose lost weight initially and then regained it. These cats had no overt signs of toxicity and were not necropsied or examined further. At 700 mg/kg, the cats stopped eating during the first week after injection, became moribund, and were euthanized. Cholinesterase activities in these cats were similar to those in the controls. No evidence of axonal degeneration, demyelination, or other adverse change was seen in sections from 11 levels of the nervous system extending from cerebral cortex to peripheral nerve in the 700 mg/kg group. The cat that received 1,000 mg/kg became anorexic 1 week after injection and was necropsied at 3 weeks after injection. Sections of this cat's brain stem and spinal cord did not reveal any abnormalities. Actual data were not presented.
Reference: Wills et al., 1979

Additional studies

Additional oral studies at lower doses in the chicken [one at 500 mg/kg in the hen (Aldridge and Barnes, 1961), and another at 1,000 mg/kg in the cockerel (young rooster) (Hine et al., 1956)] also reported no signs of delayed neurotoxicity. Two delayed neurotoxicity studies that reported some axonal lesions in the spinal cord of hens following 5,000 mg/kg/day of TPP (unknown purity) for 5 days are considered invalid because the doses were so high that most of the hens died or were killed in extremis during the study, severe weight loss occurred in the hens, and the same mild axonal lesions were seen in both controls and treated hens (Ciba-Geigy Pharmaceuticals Division, 1982), or because no controls were used (Ciba-Geigy Pharmaceuticals Division, 1981a).

Neurotoxicity (Adult)

Conclusion:

The available adult neurotoxicity data were judged adequate to meet the endpoint.

Basis for Conclusion:

The available study of neurobehavioral effects following subchronic feeding of TPP to rats (Sobotka et al., 1986) predates the guidelines, but fulfills some of the criteria for a Neurotoxicity Screening Battery. It includes some of the observations from the functional observational battery, and a few additional measures (rearing activity, rotorod, negative geotaxis). It does not include neurohistopathological examinations, and testing was conducted in only one sex rather than both sexes as recommended. In other reasonably well-conducted studies of this chemical, however, there is no evidence that one sex is significantly more sensitive than the other or that the chemical is neurotoxic. Structure-activity studies do not indicate neurotoxic potential for TPP (Johnson, 1975). Therefore, the existing study, in context with the other information regarding TPP toxicity, may be adequate to satisfy the adult neurotoxicity component of the neurotoxicity endpoint. The study description follows:

$ Neurotoxicity Screening Battery (OPPTS Harmonized Guideline 870.6200; OECD Guideline 424)

Type: Neurotoxicity screening, oral
Species, strain, sex, number: Rat, Sprague-Dawley, 10 males/dose
Doses: 0, 0.25, 0.50, 0.75, or 1.0% in the diet; 0, 161, 345, 517, or 711 mg/kg/day
Vehicle: None
Purity: 98% (commercial grade, Aldrich); homogeneity and stability of TPP diets confirmed by gas chromatography
Exposure duration, frequency: 4 months, daily

Method: Observations included food consumption, body weight, in-cage observation for overt signs, open-field exploratory behavior (motor activity and rearing), rotorod, forelimb grip strength, and negative geotaxis. Extensive statistical analysis.
Results: Overt signs and test results for neurobehavioral endpoints were not statistically significantly different in treated versus control rats. Body weight gain, but not food consumption, was statistically and toxicologically significantly lower (>10% decrease) in the 0.5, 0.75, and 1.0% dietary groups than in controls, and there was a negative dose-related linear trend for weight gain. Thus, no LOAEL for neurotoxicity was demonstrated. The NOAEL and LOAEL for effects on body weight gain were 0.25% in the diet (161 mg/kg/day) and 0.50% in the diet (345 mg/kg/day).
Reference: Sobotka et al., 1986

Developmental Neurotoxicity: Developmental Neurotoxicity Study (OPPTS Harmonized Guideline 870.6300)

Conclusion:

The available developmental neurotoxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

No studies of this type were located.

Additional neurotoxicity studies:

- Schedule-Controlled Operant Behavior (mouse or rat)
  OPPTS Harmonized Guideline 870.6500
- Peripheral Nerve Function (rodent)
  OPPTS Harmonized Guideline 870.6850
- Sensory Evoked Potentials (rat, pigmented strain preferred)
  OPPTS Harmonized Guideline 870.6855

These studies may be indicated, for example, to follow up neurotoxic signs seen in other studies, or because of structural similarity of the substance to neurotoxicants that affect these endpoints. These studies may be combined with other toxicity studies.

Conclusion: These endpoints do not appear to be applicable to TPP.

Basis for Conclusion: Although there are no studies addressing these endpoints, there are no reliable data for TPP, and no structure-activity considerations, that indicate a need for these follow-up studies.

IMMUNOTOXICITY

***Conclusion*:**

The available immunotoxicity data were judged adequate to meet the endpoint.

Basis for Conclusion:

The potential immunotoxicity of TPP was examined in a subchronic dietary study in rats (Hinton et al., 1987, reprinted as Hinton et al., 1996) which predates the guideline for immunotoxicity. This study appears to satisfy most of the requirements of the guideline, although no positive control was included, and the anti-sheep red blood cell assay is not the currently recommended assay. The study, which was negative for immunotoxicity, is summarized below.

$ Immunotoxicity (OPPTS Harmonized Guideline 870.7800)

Type: Immunotoxicity, oral subchronic
Species, strain, sex, number: Rat, Sprague-Dawley, 10 males and 10 females/dose
Doses: 0. 0.25, 0.50, 0.75, or 1.00% TPP in the diet; approximately equivalent (based on measured dosages in the related studies by Sobotka et al., 1986 and Welsh et al., 1987) to 0, 163, 343, 517, and 700 mg/kg/day. No positive control.
Purity: Aldich, 98% pure, confirmed by gas chromatography, stable under the experimental conditions of this study
Exposure duration, frequency: 120 days, daily
Method: Observations included body weight, food consumption, midterm and terminal sacrifice, necropsy, spleen and thymus weights, histopathology of spleen, thymus, and mesenteric lymph nodes, immunohistochemical evaluation of B- and T-lymphocyte regions in these tissues, total serum protein and electrophoretic analysis of serum proteins, humoral response to sheep red blood cells (relative antibody titers by hemolytic assay). Extensive statistical analysis.
Results: The only statistically significant effects were a decreased growth rate (>10% difference in body weight) during the first 4 weeks in males and females of the 1.00% dietary group, and non-dose related increases in the relative percentages of ∀-globulins in treated females and ∃-globulins in treated males, which were interpreted by the study authors as a possible sign of liver activity but of uncertain toxicological significance. Because of the lack of dose-response, these findings may not be indicative of a chemical effect. This study did not demonstrate a LOAEL for immunotoxicity. The NOAEL and LOAEL for decreased body weight gain were 0.75% in the diet (517 mg/kg/day) and 1.0% in the diet (700 mg/kg/day).
Reference: Hinton et al., 1987

GENOTOXICITY

Conclusion: The available genotoxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

Three studies of gene mutation *in vitro* report negative results. These studies, two in bacteria and one in mammalian cells, predate the relevant guidelines, but were conducted in a manner similar to them, and together, characterize the gene mutation *in vitro* endpoint. Studies of chromosomal aberrations were not available, however, and are needed for adequate characterization of the genotoxicity endpoint.

Gene Mutation in Vitro:

- **Bacterial Reverse Mutation test (OPPTS Harmonized Guideline 870.5100; OECD Guideline 471)**

Type: Bacterial reverse mutation
Species, strain: *Salmonella typhimurium* TA98, TA100, TA1535, TA1537
Metabolic activation: Tested with and without Aroclor 1254-induced liver S9 from male Syrian hamsters (10% in S9 mix for all strains and also 50% for TA1535 and TA1537), and male Sprague-Dawley rats (10% for all strains)
Concentrations: 0, 100, 333, 1,000, 3,333, and 10,000 :g/plate. Solvent was 95% ethanol. A precipitate was present in the plates at ∃3,333 ug/plate; tested in triplicate; plus replicate
Purity: 98% +
Method: Preincubation (20 minutes) and plate incorporation (48 hours) at 37EC. Positive controls were 2-aminoanthracene for all strains with S9, and sodium azide (TA1535 and TA100), 9-aminoacridine (TA1537), and 4-nitro-o-phenylenediamine (TA98) in the absence of S9.
Results: No increase over negative control at any concentration; no apparent cytotoxicity; the two highest concentrations tested may have exceeded solubility limits.
Reference: Zeiger et al., 1987

Type: Bacterial reverse mutation
Species, strain: *Salmonella typhimurium* TA98, TA100, TA1535, TA1537, TA1538
Metabolic activation: Tested with and without Aroclor 1254-induced liver S9 from male Sprague-Dawley rats
Concentrations: 0, 10, 100, 500, and 1,000 :g/plate. Solvent was DMSO; tested in triplicate; plus replicate
Purity: No data, white crystals
Method: Plate incorporation, 48 hour incubation at 37EC; apparently only one plate for each concentration. Negative and positive controls.
Results: No increase in revertants over negative control at any concentration; highest concentration reportedly produced some evidence of physiological effect. *Saccharomyces cerivisiae* D4 also tested.
Reference: Litton Bionetics, Inc., 1978a

$ **In vitro Mammalian Cell Gene Mutation Test (OPPTS Harmonized Guideline 870.5300; OECD Guideline 476)**

Type: Mammalian Cell Gene Mutation Test: Forward Mutation
Species, strain: Mouse lymphoma L5178Y
Metabolic activation: Tested with and without Aroclor 1254-induced liver S9 from male Sprague-Dawley rats
Concentrations: 0, 3.13 (only without S9), 6.26, 12.5, 25, 50, and 75 (only with S9) :g/plate. Solvent was DMSO; tested in triplicate; plus replicate
Purity: No data, white crystals
Method: Plate incorporation, 48 hour incubation at 37EC. Negative and positive controls (ethylmethanesulfonate without S9; dimethylnitrosamine with S9).
Results: No increase over negative control at any concentration; highest concentration selected during prescreening as a level that reduced growth potential.
Reference: Litton Bionetics, Inc., 1978b

Other

$ **Mitotic Gene Conversion in Saccharomyces cerevisiae (OPPTS Harmonized Guideline 870.5575)**

Type: Mitotic Gene Conversion
Species, strain: *Saccharomyces cerevisiae* D4
Metabolic activation: Tested with and without Aroclor 1254-induced liver S9 from male Sprague-Dawley rats
Concentrations: 0, 10, 100, 500, and 1,000 :g/plate. Solvent was DMSO
Purity: No data, white crystals
Method: Plate incorporation, 3- to 5-day incubation at 30EC (without S9) or 37EC (with S9). Negative and positive controls
Results: No increase over negative control at any concentration; highest concentration reportedly produced some evidence of physiological effect.
Reference: Litton Bionetics, Inc. 1978a

No studies were available on the genotoxicity of triphenyl phosphate in the following types of types of tests:

Gene Mutation in Vivo
Chromosomal Aberrations in Vitro
Chromosomal Aberrations in Vivo
DNA Damage and Repair

Ecotoxicity

Acute Toxicity to Fish (OPPTS Harmonized Guideline 850.1075; OECD Guideline 203)

Conclusion:

The available acute fish toxicity data were judged adequate to meet the endpoint.

Basis for Conclusion:

The available acute fish toxicity studies are summarized in Table 1. Acute 96-hour toxicity studies in freshwater fish species including rainbow trout, fathead minnows, goldfish, bluegill sunfish, medaka, channel catfish, and carp and in saltwater species including silverside and sheepshead minnow were located. Most of the 96-hour LC50 values reported in the available literature are consistent with each other and ranged from 300 to 1,200 :g/L. One study (Dawson et al., 1977), however, reported substantially higher LC50 values for TPP (95,000 :g/L in silverside and 290,000 :g/L in bluegill). A reason for this discrepancy is not clear. However, the data reported by Dawson et al. (1977) were considered unreliable because the reported LC50 values are approximately 50 to 150 times greater than the solubility limit of TPP (approximately 2,000 :g/L). Also, the results reported by Dawson et al. (1977) are inconsistent with results from multiple other studies.

Overall, the available acute fish toxicity endpoint appears to be satisfied by the currently existing database for the following reasons:

$ Studies are available in both cold- and warm-water freshwater species and in marine species;
$ Numerous studies are available that reported similar LC50 values; and
$ Although most of the available studies used static conditions, the results from the only study located that used flow-through conditions and analytically confirmed the test concentrations are consistent with results from static studies conducted in the same species. These data indicate that use of static exposure conditions produces similar results as flow-through studies.

It should be noted, however, that sufficient detail was not included in many of the study reports to allow for a comprehensive and independent evaluation of data adequacy, most studies used static conditions and did not analytically confirm the test concentrations, and many studies were conducted prior to publication of GLP guidelines.

A summary of the available acute toxicity studies in fish that were located as well as selected deficiencies in the studies is presented in Table 1. Studies that were either published in a foreign language or that were not readily available AND that were not critical to the hazard assessment were not retrieved.

Table 1. Summary of available acute fish toxicity studies for triphenyl phosphate (115-86-6)[a]									
			Selected Study Design Parameters						
Study Reference	**Species Tested**	**96-Hour LC50**	**Study Type**	**Concentration Range Tested**	**No. of Fish/ Conc**	**Analytical Monitoring**	**Water Chemistry[b]**	**Solvent**	**Comments on the Data**
Ahrens et al., 1978	Carp	<1,000 :g/L	Static	Not reported	10	No	**pH:** NR **Temp:** "room" temp. **DO:** NR **Hardness:** NR	Acetone (0.6 mL/L)	The study conduct followed German guidelines. Reporting deficiencies preclude an independent evaluation of data adequacy. LC50 values were not reported. LC100 was 1,000 and 10,000 :g/L with and without acetone, respectively. LC0 without acetone was 5,000 :g/L. LC0 value with acetone was not observed.
Ciba-Geigy, 1981a	Rainbow trout 49 mm; 0.94 g	850 :g/L	Static	5 concentrations; 0.18 to 1,800 :g/L	10	No	**pH:** 7.7-8.2 **Temp:** 14.5-15.6EC **DO:** 5-9 mg/L **Hardness:** 172 mg/L	Mixture of octanol (>0.004 mL/L), tween (>0.07 mL/L), and ethylene glycol monomethyl ether (>0.02 mL/L)	The study reportedly followed OECD Guideline 203. TPP purity was 100%; loading rate was 0.21 g/L. Only minor reporting deficiencies were noted. Sublethal effects included abnormal swimming behavior and loss of equilibrium at all concentrations tested.

Dawson et al., 1977	Bluegill sunfish	290,000 :g/L Water solubility is approx. 2,000 :g/L	Static	5 concentrations, 125,000 to 560,000 :g/L	Not reported	No	Dilution water was reported to have a pH of 7.6-7.9 and a hardness of 55 mg/L. Target temp. was 23EC for bluegill and 20EC for silverside	Either distilled water or solvent with (reportedly) relatively low toxicity was used. Concentration of solvent, if used, was not reported.	The reported LC50 value from this study is substantially higher than the water solubility of TPP (approx. 2,000 :g/L); therefore, these data are unreliable.
	Silverside	95,000 :g/L Water solubility is approx. 2,000 :g/L	Static	5 concentrations, 75,000 to 560,000 :g/L					
Food and Drug Research Labs, 1979	Rainbow trout	760 :g/L	Static	5 concentrations, 180 to 1,800 :g/L	10	No	**pH:** 7.2-7.5 **Temp:** 12EC∀1EC **DO:** 7.8-10 mg/L **Hardness:** 42 mg/L	Unidentified solvent	Study reportedly followed U.S. EPA (1975) guidelines. Solvent and blank controls were used. Loading rate was 0.15 g/L.
	Fathead minnow	3,800 :g/L Water solubility is approx. 2,000 :g/L	Static	5 concentrations, 1,000 to 10,000 :g/L	10	No	**pH:** 6.8-7.5 **Temp:** 20.6∀0.6EC **DO:** 1.3-9.0 mg/L **Hardness:** 43 mg/L	Unidentified solvent	Dissolved oxygen concentrations decreased over the course of the study to as low as 1.3 mg/L. The LC50 determined from this study was greater than the water solubility of TPP.

Geiger et al., 1986	Fathead minnow (17 mm; 0.071 g)	870 :g/L	Flow-through (14.4x per day)	5 concentrations; 180 to 1,150 :g/L (mean measured)	20	Yes (GLC; 99.8% recovery)	**pH:** 7.8 **Temp:** 24.5EC **DO:** 6.4 mg/L **Hardness:** 45.6 mg/L Values are averages over the study duration; ranges were not reported	None used; 1.2 mg/L stock solution in glass wool column	Fish were 29 days old at study initiation. Loading rate was 1.4 g/L, and purity was 98%. In the high-dose group, 19/20 fish were dead by the 24-hour observation, and the remaining fish was dead by the 48-hour observation period. Reporting deficiencies included lack of water chemistry parameter values (e.g., pH, dissolved oxygen, temperature) at each concentration (although mean values were given), and a solvent was not used.
Huckins et al., 1991	Bluegill sunfish (0.5-1 g)	780 :g/L	Static	5 concentrations, 500 to 10,000 :g/L with and without addition of 1 g/L soil and clay	10	No	**pH:** NR **Temp:** 22EC **DO:** NR **Hardness:** NR	Acetone, unspecified concentration	TPP purity was 99%. Selected reporting deficiencies included concentration of solvent used, pH and dissolved oxygen of the test system during the study, and loading rate.

Industrial Bio Test Labs, Inc., 1972	Rainbow trout	Between 100 and 1,000 :g/L	Static	4 concentrations; 100 to 100,000 :g/L	Not reported	No	**pH:** 7.3-7.9 **Temp:** 12.2EC **DO:** 2.9-7.9 mg/L **Hardness:** NR	Acetone	Very limited information on the study was available. Data were obtained from unpublished EPA submission from TSCATS. Reporting deficiencies preclude an independent evaluation of data adequacy.
	Bluegill sunfish	Between 1000 and 10,000 :g/L Water solubility is approx. 2,000 :g/L	Static	4 concentrations; 100 to 100,000 :g/L	Not reported	No	**pH:** 7.6-8.2 **Temp:** 18.6EC **DO:** 6.9-7.5 mg/L **Hardness:** NR	Acetone	

Mayer et al., 1981 EG&G Bionomics, 1978a, b	Rainbow trout	400 µg/L	Static	Not reported	10	No	pH: 7.2 Temp: 12.1°C DO: NR Hardness: 272 mg/L	**Not reported**	Data were obtained from Mayer et al., 1981 and from unpublished data reported in TSCATS. Fish age, weight, and length and loading rate were not reported.
	Fathead minnow	660 µg/L	Static	3 concentrations; 280 to 2200 □g/L	10	No	pH: 6.3-7.5 Temp: 22.1°C DO: 2.5-8.7 mg/L Hardness: 28-44 mg/L	**Triethylene glycol (up to 7.5 mL)**	Data were obtained from Mayer et al., 1981 and from unpublished data reported in TSCATS. Fish age, weight, and length and loading rate were not reported.
	Sheeps-head minnow	Between 320 and 560 µg/L	Static	5 concentrations; 56 to 560 □g/L	10	No	pH: 7.9-8.1 Temp: 20.1°C DO: 3.8-6.3 mg/L Hardness: NR Salinity: 17 parts per thousand	**Acetone**	Data were obtained from Mayer et al., 1981 and from unpublished data reported in TSCATS. Fish age, weight, and length and loading rate were not reported.

Mayer and Ellersieck, 1986	Rainbow trout	370 µg/L	Static	Not reported	Not reported	Yes	pH: 7.4 Temp: 12°C DO: NR Hardness: 40 mg/L	**Not reported**	Results of analytical monitoring were not reported. General methods were reported in the publication that were not necessarily specific for the test on TPP.
	Channel catfish	420 µg/L	Static	Not reported	Not reported	Yes	pH: 7.5 Temp: 22°C DO: NR Hardness: 38 mg/L	**Not reported**	Results of analytical monitoring were not reported. General methods were reported in the publication that were not necessarily specific for the test on TPP.
	Fathead minnow	1,000 µg/L	Static	Not reported	Not reported	Yes	pH: 7.3 Temp: 22°C DO: NR Hardness: 44 mg/L	**Not reported**	Results of analytical monitoring were not reported. General methods were reported in the publication that were not necessarily specific for the test on TPP.
Palawski et al., 1983	Rainbow trout (0.11 g; 24 mm)	360 µg/L	Static	3 concentrations; 210, 240, and 290 □g/L	10	No	pH: NR Temp: NR DO: NR Hardness: NR	**Not reported**	TPP was 99% pure. The study followed U.S. EPA (1975) guidelines. Fry, 12 days past swim-up stage, were tested. An EC50 based on immobility, mortality, and loss of equilibrium of 300 :g/L was also determined from this study.

Sasaki et al., 1981	Goldfish (0.8-2.8 g) Killifish (0.1-0.2 g)	700 µg/L 1200 µg/L	Static Static	Not reported Not reported	7 to 9 7 to 9	No* *In a parallel study, 70% of TPP was present in water that contained goldfish after 96 hours.	pH: NR Temp: 25°C DO: NR Hardness: NR	**Not reported**	Neither goldfish nor killifish are recommended species for testing by OECD 203. Reporting deficiencies preclude an independent evaluation of data adequacy. Selected reporting deficiencies included: water chemistry values (pH, hardness, dissolved oxygen), identification of test concentrations, and use of a vehicle to facilitate dissolution. Spine deformation occurred at 1.1 mg/L.
Sitthichai-kasem., 1978	Rainbow trout sac-fry (0.081 g) Rainbow trout fingerlings (0.75 g)	389 µg/L 299 µg/L	Static Static	Control and 180-1000 □g/L Control and 180-1000 □g/L	10 10	No No	pH: 7.0-7.2 Temp: 12°C DO: 7.3-8.5 ppm Hardness: 40-48	**Acetone** **Acetone**	Fish were acclimated before exposure. Moribund and dead fish were counted at 24, 48, 72, and 96 hours.

[a]Studies that were either published in a foreign language or that were not readily AND that were not critical to the hazard assessment were not retrieved.
[b]Hardness reported as mg/L $CaCO_3$

Acute Toxicity to Freshwater and Marine/Estuary Invertebrates (OPPTS Harmonized Guidelines 850.1010 and 850.1035; OECD Guideline 202)

Conclusion:

- $ The available acute freshwater invertebrate toxicity data were judged adequate to meet the endpoint.
- $ The available acute marine/estuary invertebrate toxicity data was judged inadequate to meet the endpoint.
- $ Based on the environmental fate of TPP, additional data may be needed on sediment dwelling organisms. Currently available studies, although inadequate to satisfy the endpoint in this review, indicate that TPP may be toxic to sediment-dwelling organisms.

Basis for Conclusion:

Freshwater Organisms

The available data are summarized in Table 2. Four studies in daphnids were located. All studies used static conditions, and none of the available studies analytically confirmed the test concentrations. The reported EC50 values were consistent with each other and ranged from 1,000 to 1,350 :g/L. Sufficient detail was available from three of the four studies located to allow for an independent evaluation of data adequacy. Reporting deficiencies were noted in those three studies that included lack of identity of concentrations tested, TPP purity, concentration of solvent in the test solutions, and water hardness. In the remaining study (Ziegenfuss et al., 1986), even basic study design parameters were not reported. Due to these reporting deficiencies and on study design deficiencies (lack of analytical confirmation of the test concentrations), none of the currently available studies are independently sufficient to be used as the basis to satisfy the acute freshwater invertebrate toxicity endpoint. Collectively, however, the data appear adequate because the four studies that were located reported a narrow range of EC50 values, thus providing confidence in the reported effect levels.

Studies were also located on the toxicity of sediment-dwelling organisms. Two studies using the midge and one study using the scud were located. These studies indicate that sediment-dwelling organisms could be particularly sensitive to the toxicity of TPP. EC50 values ranged from 250 to 1,600 :g/L. All of the studies in sediment-dwelling organisms used static conditions, and none of the studies analytically confirmed the test concentrations. Based on the inconsistencies in the reported toxicity values and the lack of a study that analytically confirmed the test substance concentrations, the currently available data do not appear to be adequate to satisfy the acute toxicity endpoint for sediment-dwelling organisms. Based on the environmental fate of TPP, additional testing on sediment-dwelling organisms may be needed.

Marine/Estuarine Organisms

One acute toxicity study in mysid shrimp was located (Table 2). The study was a 96-hour static study that did not analytically confirm the test concentrations. The dissolved oxygen concentration in this study was <60% of saturation after the 96-hour exposure period. The LC50 from this study was between 180 and 320 :g/L; a discrete LC50 was not calculated. The available data in mysid shrimp do not appear to be adequate to satisfy the marine/estuarine invertebrate toxicity endpoint because only one publicly available study was located, and it used static conditions, did not analytically confirm the test concentrations, and dissolved oxygen concentration in this study was below values recommended by standard guidelines. Because only one study was available, and it of questionable reliability, the marine/estuarine invertebrate toxicity endpoint does not appear to be satisfied by existing data.

Table 2. Summary of available acute invertebrate toxicity studies on triphenyl phosphate (115-86-6)									
Study Reference	**Species Tested**	**EC50 or LC50 (:g/L)**	**Selected Study Design Parameters**						**Comments on the Data**
			Study Type	**Concentration Range Tested**	**No. of Organisms/ Conc**	**Analytical Monitoring**	**Water Chemistry**	**Solvent**	
Ciba-Geigy Ltd., 1981b	Daphnid	48-hour: 1,350	Static	800-3,700 :g/L	20	No	**pH:** 8.6 **DO:** 7.0-7.2 mg/L **Temp:** 20∀1EC **Hardness:** NR	DMF	Although reporting deficiencies were noted, the study conduct appears to be consistent with current standard guidelines. pH and dissolved oxygen were only measured at test termination and only at the lowest and highest test concentrations. TPP purity was not reported.

Table 2. Summary of available acute invertebrate toxicity studies on triphenyl phosphate (115-86-6)									
Study Reference	**Species Tested**	**EC50 or LC50 (:g/L)**	**Selected Study Design Parameters**						**Comments on the Data**
			Study Type	**Concentration Range Tested**	**No. of Organisms/ Conc**	**Analytical Monitoring**	**Water Chemistry**	**Solvent**	
Food and Drug Research Labs, 1979	Daphnid	48-hour: 1,280	Static	180-3,200 :g/L	20	No	**pH:** 8.4-8.5 **DO:** 7.8-9.4 mg/L **Temp:** 20∀0.5EC **Hardness:** 232 mg/L	Acetone	Although reporting deficiencies exist, the details that were reported appear to be consistent with current guidelines. Key deficiencies included lack of analytical monitoring of the test concentrations. TPP purity was not reported.

Table 2. Summary of available acute invertebrate toxicity studies on triphenyl phosphate (115-86-6)									
Study Reference	**Species Tested**	**EC50 or LC50 (:g/L)**	**Selected Study Design Parameters**						**Comments on the Data**
			Study Type	**Concentration Range Tested**	**No. of Organisms/ Conc**	**Analytical Monitoring**	**Water Chemistry**	**Solvent**	
Mayer et al., 1981 Analytical Bio Chemistry Labs, 1978	Daphnid	48-hour: 1,000	Static	Not reported	10	No	**pH:** 7.7-8.0 **DO:** 7.2-8.7 **Temp:** 19EC **Hardness:** <250 mg/L	Ethanol	Only 10 daphnids were exposed to each concentration. Otherwise, the details reported on the study conduct appear to be consistent with current standard guidelines. The concentrations tested were not identified. TPP purity was not reported.
Ziegenfuss et al., 1986	Daphnid	48-hour: 1,000	Static	Not reported	Not reported	No	**pH:** NR **DO:** NR **Temp:** NR **Hardness:** NR	Not reported	Even basic study design parameters were not available for evaluation.

Table 2. Summary of available acute invertebrate toxicity studies on triphenyl phosphate (115-86-6)									
Study Reference	**Species Tested**	**EC50 or LC50 (:g/L)**	**Selected Study Design Parameters**						**Comments on the Data**
			Study Type	**Concentration Range Tested**	**No. of Organisms/ Conc**	**Analytical Monitoring**	**Water Chemistry**	**Solvent**	
Huckins et al., 1991	Midge	48-hour: 360	Static	60-1,000 :g/L	10	No	**pH:** NR **DO:** NR **Temp:** 22EC **Hardness:** NR	Acetone	Study reportedly followed U.S. EPA (1975) guidelines. Results from monitoring water quality parameters were not reported.
Ziegenfuss et al., 1986 Monsanto Env. Science Section, 1982	Midge	48-hour: 1,600	Static	125-2,000 :g/L	10	No	**pH:** 7.6-8.1 **DO:** 8.6-9.3 **Temp:** 21-23EC **Hardness:** 268-284 mg/L	Unspecified solvent	The NOAEC was 1,000 :g/L. The study followed U.S. EPA (1975) guidelines.

Table 2. Summary of available acute invertebrate toxicity studies on triphenyl phosphate (115-86-6)									
Study Reference	**Species Tested**	**EC50 or LC50 (:g/L)**	**Selected Study Design Parameters**						**Comments on the Data**
			Study Type	**Concentration Range Tested**	**No. of Organisms/ Conc**	**Analytical Monitoring**	**Water Chemistry**	**Solvent**	
Huckins et al., 1991	Scud	96-hour: 250	Static	10-560 :g/L	Not reported	No	**pH:** NR **DO:** NR **Temp:** 17EC **Hardness:** NR	Acetone	Study reportedly followed U.S. EPA (1975) guidelines. Reporting deficiencies preclude an independent evaluation of data adequacy.
Mayer et al., 1981 EG&G Bionomics. 1978c	Mysid shrimp	96-hour: >180 and <320	Static	56-560 :g/L	10	No	**pH:** 7.8-7.9 **DO:** 43%-56% of saturated **Temp:** 20∀1EC **Hardness:** NR	Acetone (1 mL)	Dissolved oxygen was <60% of saturation. Standard guidelines indicate that dissolved oxygen concentration remain >60% saturation throughout the study.

Table 2. Summary of available acute invertebrate toxicity studies on triphenyl phosphate (115-86-6)									
Study Reference	**Species Tested**	**EC50 or LC50 (:g/L)**	**Selected Study Design Parameters**						**Comments on the Data**
			Study Type	**Concentration Range Tested**	**No. of Organisms/ Conc**	**Analytical Monitoring**	**Water Chemistry**	**Solvent**	
Lo and Hsieh, 2000	Golden apple snail	72-hour: 38,200	Static	10-250 :g/L	30	Yes	**pH:** 7.5 **DO:** NR **Temp:** 26EC **Hardness:** NR	Not reported	Organisms were 35-40 days old at study initiation. Golden apple snail is not a common test organism.

Algal Toxicity (OPPTS Harmonized Guideline 850.5400; OECD Guideline 201)

Conclusion:

The available algal toxicity data were tentatively judged adequate to meet the endpoint, pending the availability of additional information from the studies that were not included in the published articles.

Basis for Conclusion:

Seventy-two-hour static studies in *Selenastrum capricornutum*, *Scenedesmus subspicatus*, *Chlorella vulgaris* (Millington et al., 1988), a 96-hour static study in *Selenastrum capricornutum* (Mayer et al., 1981), and a 22-day study in *Ankistrodesmus falcatus* were located. These data are summarized in Table 3. Taken together, these data may be adequate; however, additional information is needed from the studies before they can be used as the basis for satisfying the algal toxicity endpoint.

Millington et al. (1988) conducted a series of 72-hour static studies that were designed to evaluate the influence of various standard test media (OECD, U.S. EPA, and Bold's basal) on the toxicity of triphenyl phosphate to three algal species, *Selenastrum capricornutum*, *Scenedesmus subspicatus*, and *Chlorella vulgaris*. These static studies followed OECD Guideline 201. Five concentrations ranging from 0.05 to 5 mg/L were tested in triplicate cultures. The test concentrations were not analytically confirmed. The resulting 72-hour NOAEC values ranged from 0.1 to 1 mg/L depending on the algal species tested and the test media used. EC50 values were not derived, and raw data were not available to allow for an independent calculation of EC50 values. Overall, the studies appear to have been adequately conducted. Deficiencies in the data included reporting deficiencies (e.g., raw data, water quality values determined during the study, and growth of control replicates), lack of analytical confirmation of the test concentrations, and lack of EC50 determinations. Provided that the missing study details can be obtained and that an EC50 value can be determined, these data appear adequate to satisfy the algal toxicity endpoint.

Mayer et al. (1981) conducted a 96-hour static test in *Selenastrum capricornutum*. Many details from this study were obtained from the unpublished report submitted to EPA (EG&G Bionomics, 1978d). Five concentrations that ranged from 0.6 to 10 mg/L were tested. Test concentrations were not analytically confirmed. An EC50 of 2 mg/L (95% confidence interval of 0.6-4 mg/L) was derived from this study. A clear NOAEC was not established because a 4% decrease in cell number and a 15% decrease in chlorophyll-∀ concentration was observed at the lowest concentration of 0.6 mg/L. Although the study appears to have been adequately conducted, initial and final cell concentrations of controls or treated cultures were not reported. Provided that these study details can be obtained, the 96-hour EC50 reported in this study appears to be adequate to satisfy the short-term algal toxicity endpoint. It should be noted that the EC50

determined from this study is at the approximate water solubility limit of TPP (2 mg/L). The lack of a clear NOAEC precludes the use of this study as the sole basis to satisfy the chronic algal toxicity endpoint. However, the low magnitude of the effect observed at 0.6 mg/L in this study appears to be consistent with the NOAEC and LOAEC values reported in the other algal toxicity studies (Mayer et al., 1981; Wong and Chau, 1984).

Wong and Chau (1984) reported a 22-day NOAEC of 0.1 mg/L and a LOAEC of 0.5 mg/L based on algal growth in *Ankistrodesmus falcatus*. Sufficient detail was not reported in this study to allow for an independent evaluation of data adequacy. Virtually no details on the methods or results were reported. The study also reported 4-hour IC50 values based on incorporation of radiolabeled CO_3 as an indication of primary productivity. These IC50 values ranged from 0.2 to 0.5 mg/L in *Ankistrodesmus falcatus*, *Scenedesmus quadricauda*, and Lake Ontario phytoplankton. The 4-hour IC50 values derived from this study were not considered adequate for this hazard assessment because TPP concentrations that caused reductions in primary productivity after 4 hours of exposure did not affect reproduction or growth during a separate 22-day study conducted by the same laboratory. The NOAEC and LOAEC values derived from the 22-day study were considered inadequate to satisfy the chronic algal toxicity endpoint because sufficient detail was not available on the study design or results to allow for an independent evaluation of study adequacy. However, if data are available to demonstrate that the study was adequately conducted, then the data may be sufficient to satisfy the chronic algal toxicity endpoint. Further, if concentration-response data are available to allow for a calculation of a 96-hour EC50, then the data may also be used to support the short-term algal toxicity endpoint.

Taken together, it appears that sufficient data are available to satisfy the algal toxicity endpoint; however, additional information is needed before the currently available data can be considered adequate.

Table 3. Summary of available algal toxicity studies for triphenyl phosphate								
Study Reference	**Species Tested**	**EC50, NOAEC, and LOAEC**	**Selected Study Design Parameters**					**Comments on the Data**
			Study Type	**Concentration Range Tested**	**Analytical Monitoring**	**Water Chemistry**	**Solvent**	
Millington et al., 1988	*Selenastrum capricornutum*	**EC50**: NR **72-hour NOAEC:** 0.1-1 mg/L* **72-hour LOAEC:** 0.5-5 mg/L* *A range of NOAEC and LOAEC values is reported because tests were performed using three different test media, and the toxicity of TPP was influenced by the test media used.	Static	0.05-5 mg/L	No	**pH:** NR **Temp:** 22EC **DO:** NR **Hardness:** NR	Acetone (<100 uL/L)	The 72-hour LOAEC was between 0.5 and 5 mg/L depending on the test medium. EC50 values were not determined. Test substance purity was not reported.

Table 3. Summary of available algal toxicity studies for triphenyl phosphate								
Study Reference	**Species Tested**	**EC50, NOAEC, and LOAEC**	**Selected Study Design Parameters**					**Comments on the Data**
			Study Type	**Concentration Range Tested**	**Analytical Monitoring**	**Water Chemistry**	**Solvent**	
Millington et al., 1988	*Scenedesmus subspicatus*	**72-hour NOAEC:** 0.1-1 mg/L* **72-hour LOAEC:** 0.5-5 mg/L. *A range of NOAEC and LOAEC values is reported because tests were performed using three different test media, and the toxicity of TPP was influenced by the test media used.	Static	0.05-5 mg/L	No	**pH:** NR **Temp:** 22EC **DO:** NR **Hardness:** NR	Acetone (<100 uL/L)	The 72-hour LOAEC was between 0.5 and 5 mg/L depending on the test medium. EC50 values were not determined. Test substance purity was not reported.

Table 3. Summary of available algal toxicity studies for triphenyl phosphate								
Study Reference	**Species Tested**	**EC50, NOAEC, and LOAEC**	**Selected Study Design Parameters**					**Comments on the Data**
			Study Type	**Concentration Range Tested**	**Analytical Monitoring**	**Water Chemistry**	**Solvent**	
Millington et al., 1988	*Chlorella vulgaris*	**72-hour NOAEC:** 1 mg/L **72-hour LOAEC:** 5 mg/L The toxicity of TPP to Chlorella vulgaris was not affected by test medium.	Static	0.05-5 mg/L	No	**pH:** NR **Temp:** 22EC **DO:** NR **Hardness:** NR	Acetone (<100 uL/L)	The 72-hour LOAEC was 5 mg/L using three different test mediums. EC50 values were not determined. Test substance purity was not reported.

Table 3. Summary of available algal toxicity studies for triphenyl phosphate

Study Reference	Species Tested	EC50, NOAEC, and LOAEC	Selected Study Design Parameters					Comments on the Data
			Study Type	Concentration Range Tested	Analytical Monitoring	Water Chemistry	Solvent	
Mayer et al., 1981 EG&G Bionomics, 1978d	*Selenastrum capricornutum*	96-hour: 2 mg/L 95% CI: 0.6-4 96-hour LOAEC: 0.6 mg/L 96-hour NOAEC: Not observed	Static	0.6-10 mg/L	No	**pH:** 7.0-8.2 **Temp:** 24∀1EC **DO:** NR **Hardness:** NR	Acetone: 0.05 mL	The methods reportedly followed U.S. EPA, 1971 guidelines. Control growth was not reported. A NOAEC did not appear to be observed because a 15% decrease in chlorophyll ∀ and 4% decrease in cell number was observed after 96 hours at the lowest concentration of 0.6 mg/L. Test substance purity was not reported.

Table 3. Summary of available algal toxicity studies for triphenyl phosphate

Study Reference	Species Tested	EC50, NOAEC, and LOAEC	Selected Study Design Parameters					Comments on the Data
			Study Type	Concentration Range Tested	Analytical Monitoring	Water Chemistry	Solvent	
Wong and Chau, 1984	*Ankistrodesmus falcatus*	22-day NOAEC: 0.1 mg/L 22-day LOAEC: 0.5 mg/L	Static	0.05-5 mg/L	No	**pH:** NR **Temp:** NR **DO:** NR **Hardness:** NR	5 :L	Use of standard guidelines was not indicated. Duplicate cultures were used. Virtually no study details were included in the published article, precluding an independent evaluation of data adequacy. Growth of *A. falcatus* was determined spectrophotometrically. Test substance purity was not reported.

Chronic Toxicity to Fish (OPPT Harmonized Guideline 850.1400; OECD Guideline 210)

Conclusion:

The available chronic toxicity data for freshwater or saltwater fish were judged inadequate to meet the endpoint.

Basis for Conclusion:

Freshwater Fish

The available data are summarized in Table 4. Two chronic studies in fish were located. Both studies were published in Mayer et al. (1981). The study in fathead minnows reported a NOAEC of 87 :g/L and a LOAEC of 230 :g/L. The study used flow-through conditions and analytically confirmed the test concentrations; however, the study is considered invalid due to the large variation in measured concentrations (55-170 :g/L at the NOAEC and 140-390 :g/L at the LOAEC). The study in rainbow trout is considered to be inadequate because the highest concentration tested was 1.4 :g/L, a concentration that did not elicit any effects. Also, the measured concentrations were not given. Therefore, validity of the test could not be independently evaluated.

Saltwater Fish

No chronic toxicity studies in saltwater fish species were located.

Table 4. Summary of available chronic fish toxicity studies for triphenyl phosphate (115-86-6)									
			Selected Study Design Parameters						
Study Reference	**Species Tested**	**NOAEC/ LOAEC**	**Study Type**	**Concentration Range Tested**	**No. of Fish/ Conc**	**Analytical Monitoring**	**Water Chemistry**	**Solvent**	**Comments on the Data**
Mayer et al., 1981	Rainbow trout	90-day LOAEC: >1.4 :g/L	Flow-through (20 L/hour)	Nominal: 0.22, 0.38, 0.44, 0.64, 0.91, 1.2, and 1.4 :g/L Measured concentrations not reported	NR, but at least 10 based on the number of fish subjected to vertebrae pathology exams.	Yes (mean measured concentrations were within 62% of nominal)	**pH:** 7.2 **Temp:** 12∀1EC **DO:** NR **Hardness:** 272 mg/L	Unidentified solvent at <0.05 mL/L	Measured concentrations were not reported. Endpoints evaluated included mortality, behavior, weight, length, vertebrae pathology, and eye pathology. Test substance purity was not reported.
Mayer et al., 1981 EG&G Bionomics, 1979	Fathead minnow	30-day NOAEC: 87 :g/L LOAEC: 230 :g/L	Flow-through (20 L/hour)	Mean measured: 0, 2.8, 12, 36, 87, and 230 :g/L	60 eggs 40 fry	Yes	**pH:** 6.8-7.6 **Temp:** 25∀1EC **DO:** >75% saturation **Hardness:** 38-44 mg/L	TEG, unspecified concentration	Results based on fry survival; other parameter were not affected by treatment. Measured concentrations varied substantially and ranged from 55 to 170 :g/L at the NOAEL and from 140 to 390 :g/L at the LOAEL. Test substance purity was not reported.

Chronic Toxicity to Aquatic Invertebrates (OPPTS Harmonized Guidelines 850.1300 and 850.1350; OECD Guideline 211)

Conclusion:

The available chronic toxicity data for freshwater or saltwater invertebrates were judged inadequate to meet the endpoint.

Basis for Conclusion:

Freshwater and Saltwater Species

No chronic toxicity studies in freshwater or saltwater invertebrate species were located.

Acute Oral, Acute Dietary, and Reproductive Toxicity in Birds (OPPTS Harmonized Guidelines 850.2100, 850.2200, and 850.2300; OECD Guidelines 205 and 206)

Conclusion:

The available acute oral, acute dietary and reproduction toxicity data for birds were judged inadequate to meet the endpoints.

Basis for Conclusion:

No toxicity studies in relevant bird species were located.

Earthworm Toxicity (OPPTS Harmonized Guideline 850.6200)

Conclusion:

The available data were judged inadequate to meet the earthworm toxicity endpoint.

Basis for Conclusion:

No toxicity studies in earthworms were located.

Physical/Chemical Properties

Triphenyl phosphate
CAS 115-86-6
MF $C_{18}H_{15}O_4P$
MW 326.29
SMILES c1ccccc1OP(=O)(Oc2ccccc2)Oc3ccccc3

Physical/Chemical Properties

Water Solubility (mg/L):

Conclusion:

The available water solubility data are adequate.

Basis for Conclusion:

The two best-documented studies, including one that followed an OECD-guideline test, report solubilities of 1.9-2.1 ppm.

Solubility (mg/L)	**Reference**
Insoluble	Budavari, 2001 (The Merck Index); Lewis, 2000 (Sax's Dangerous Properties of Industrial Materials); Lide and Milne, 1995 (CRC Handbook of Data on Common Organic Compounds); Lewis, 1997 (Hawley's Condensed Chemical Dictionary)
1.90	Saeger et al., 1979 (shake-flask method using Milli-Q purified water); Huckins et al., 1991; SRC, 2004 (PHYSPROP database)
2.1∀0.1	Ofstad and Sletten, 1985 (OECD Guideline 105 (column-elution) from a mixture at 25EC)
1.4-1.6	Howard and Deo, 1979 (in buffered distilled water, pH 4.4-9.5 at 21EC)
0.2-0.3	Howard and Deo, 1979 (in filtered lake or river water, pH 7.8-8.2 at 21EC)
0.73	Hollifield, 1979

Solubility (mg/L)	Reference
0.714	Kuhne et al., 1995

Log K_{ow}:

Conclusion:

The available log K_{ow} data are adequate.

Basis for Conclusion:

A variety of reputable studies report log K_{ow} values in the range of 4.5-4.7.

Log K_{ow}	Reference
4.59	SRC, 2004 (PHYSPROP database); Hansch et al., 1995
3.9	Unpublished data cited in Bengtsson et al., 1986
4.61	Mayer et al., 1981; Huckins et al., 1991
4.63	Saeger, 1979 (shake-flask method)
4.67	FMC Industrial Chemical Division, 1979 (shake-flask method)
4.58	Ciba-Geigy, Ltd., 1982
4.62	Monsanto Chemical Co., 1982a Monsanto Chemical Co., 1982b

Melting Point:

Conclusion:

The available melting point data are adequate.

Basis for Conclusion:

Melting point values within the range of 49-52EC are reported in a variety of reputable secondary sources.

Melting Point (EC)	Reference
50	Lewis, 1997 (Hawley's Condensed Chemical Dictionary); SRC, 2004 (PHYSPROP database)
49-50	Budavari, 2001 (The Merck Index); Lewis, 2000 (Sax's Dangerous Properties of Industrial Materials)
50.5	Lide and Milne, 1995 (CRC Handbook of Data on Common Organic Compounds)
50.4	Ciba-Geigy, Ltd., 1982
50-52	Sigma-Aldrich, 2003-2004
49.5-50	Dorby and Keller, 1957

Boiling Point:

Conclusion:

The available boiling point data are adequate.

Basis for Conclusion:

Most sources report reduced-pressure boiling points of 244-245EC at 10 or 11 torr for triphenyl phosphate. Perry and Green (1984) report a boiling point of 413.5EC at 760 torr, which is consistent with the boiling point extrapolated using the Clausius-Clapeyron Equation and the parameters measured by Dorby and Keller (1957). It has also been reported that triphenyl phosphate decomposes at or near its boiling point (Dorby and Keller, 1957).

Boiling Point (EC/torr)	Reference
245/11	Lewis, 1997 (Hawley's Condensed Chemical Dictionary); SRC, 2004 (PHYSPROP database); Budavari, 2001 (The Merck Index); Lewis, 2000 (Sax's Dangerous Properties of Industrial Materials); Lide and Milne, 1995 (CRC Handbook of Data on Common Organic Compounds)
244/10	Sigma-Aldrich, 2003-2004

Boiling Point (EC/torr)	Reference
413.5/760	Perry and Green, 1984
414/760 dec. >410	Dorby and Keller, 1957 (Extrapolated according to the Clausius-Clapeyron Equation using experimentally-derived parameters: Log P(torr) = -A/T + C, where T is in Kelvin, A= 4253, C=9.07) The decomposition temperature was reported in this same paper.

Vapor Pressure (torr):

Conclusion:

The available vapor pressure data are adequate.

Basis for Conclusion:

Results from the Clausius-Clapeyron equation as measured by Dorby and Keller (1957) are consistent with the vapor pressure data provided in Perry and Green (1984).

Vapor Pressure (torr/EC)	Reference
6.28×10^{-6}/25 0.90/193.5 8.6/249.8 84.7/322.5 354/379.2	SRC, 2004 (PHYSPROP database, extrapolated); Dorby and Keller, 1957 (Extrapolated according to the Clausius-Clapeyron Equation using experimentally-derived parameters Log P (torr) = -A/T + C, where T is in Kelvin, A= 4253, C=9.07)
1/193.5	Lewis, 2000 (Sax's Dangerous Properties of Industrial Materials)
1/193.5 5/230.4 10/249.8 20/269.7 40/290.3 60/305.2 100/322.5 200/349.8 400/379.2 760/413.5	Perry and Green, 1984

Odor:

Conclusion:

The odor of this compound has been adequately characterized.

Odor	Reference
Odorless	Lewis, 2000 (Sax's Dangerous Properties of Industrial Materials)
Slight aromatic odor resembling phenol Phenol-like odor	HSDB, 2004

Oxidation/Reduction:

Conclusion:

The currently available data are not adequate to satisfy the oxidation/reduction endpoint.

Basis for Conclusion:

No data are available for the oxidation/reduction endpoint.

Oxidation/Reduction Chemical Incompatibility:

Conclusion:

The currently available data are not adequate to satisfy the oxidation/reduction chemical incompatibility endpoint.

Basis for Conclusion:

No data are available for the oxidation/reduction chemical incompatibility endpoint.

Flammability:

Conclusion:

The flammability (as the flash point) has been adequately characterized.

Basis for Conclusion:

Similar values are reported in several reputable secondary sources.

Flash Point	Reference
435EF (223EC)	Sigma-Aldrich, 2003-2004
428EF (220EC)	Lewis, 1997 (Hawley's Condensed Chemical Dictionary)
428EF (cc)	Lewis, 2000 (Sax's Dangerous Properties of Industrial Materials)

Explodability:

Conclusion:

The currently available data are not adequate to satisfy the explodability endpoint.

Basis for Conclusion:

No data are available for the explodability endpoint.

Corrosion Characteristics:

Conclusion:

The currently available data are not adequate to satisfy the corrosion characteristics endpoint.

Basis for Conclusion:

No data are available for the corrosion characteristics endpoint.

pH:

Conclusion:

The currently available data are not adequate to satisfy the pH endpoint.

Basis for Conclusion:

No data are available for the pH endpoint.

UV/VIS Absorption:

Conclusion:

The UV/VIS absorption of this compound has been adequately characterized.

Basis for Conclusion:

Absorption maxima and coefficients are available for this compound in three solvent systems, and are reported in reputable sources.

Wavelength	Absorption Coefficient	Solvent	Reference
268 nm	912	Hexane	Lide and Milne, 1995 (CRC Handbook of Data on Common Organic Compounds)
262 nm	1175	Hexane	Lide and Milne, 1995 (CRC Handbook of Data on Common Organic Compounds)
256 nm	955	Hexane	Lide and Milne, 1995 (CRC Handbook of Data on Common Organic Compounds)
288 nm	$7.03x10^3$ l/mol-cm	MeOH, KOH	Sadtler Standard Spectra, no date No absorption above 320 nm
237 nm	$2.62x10^4$ l/mol-cm	MeOH, KOH	Sadtler Standard Spectra, no date No absorption above 320 nm
268.5 nm	$2.36x10^3$ l/mol-cm	MeOH	Sadtler Standard Spectra, no date No absorption above 290 nm
273.5 nm	$2.36x10^3$ l/mol-cm	MeOH, HCl	Sadtler Standard Spectra, no date No absorption above 290 nm
218 nm	$1.78x10^4$ l/mol-cm	MeOH, HCl	Sadtler Standard Spectra, no date No absorption above 290 nm

Viscosity:

Conclusion:

The currently available data are not adequate to satisfy the viscosity endpoint.

Basis for Conclusion:

No data are available for the viscosity endpoint.

Density/Relative Density/Bulk Density:

Conclusion:

The density of this compound has been adequately characterized.

Basis for Conclusion:

Similar values for density and relative density are available for this material at different temperatures. Bulk density is also reported in a reputable source.

Density	Reference
1.268 g/cc (60EC)	Lewis, 1997 (Hawley's Condensed Chemical Dictionary)
Bulk: 10.5 lb/gal	Lewis, 1997 (Hawley's Condensed Chemical Dictionary)
1.2055 g/cc (50EC)	Lide and Milne, 1995 (CRC Handbook of Data on Common Organic Compounds)
Specific gravity, 25EC: 1.2	Cited from Midwest Research Institute, 1979 in Huckins et al., 1991

Dissociation Constant in Water:

Conclusion:

This endpoint is adequately characterized

Basis for Conclusion:

TPP is not expected to dissociate under environmentally important conditions.

Henry's Law Constant:

Conclusion:

The Henry's Law Constant has been adequately characterized for this compound.

Basis for Conclusion:

One measured and one estimated value are reported in the literature, and are in reasonable agreement with one another. The estimated value is based on measured vapor pressure and water solubility data.

Henry's Law Constant	Reference
$1.2x10^{-5}$ atm-m^3/mole	Cited from Mayer et al., 1981 in Huckins et al., 1991
$3.31x10^{-6}$ atm-m^3/mole	SRC, 2004 (PHYSPROP database, estimated from vapor pressure and water solubility)

Environmental Fate

Bioconcentration

Fish:

Conclusion:

The bioconcentration of TPP has been adequately measured in rainbow trout, goldfish, and killifish.

Basis for Conclusion:

Similar BCFs are reported for rainbow trout in two key 90-day studies (Monsanto Chemical Company, 1982c; Mayer, 1981). Other studies (Muir, 1984; Muir et al., 1980) are available, but exhibit significant scatter in the data for rainbow trout. The data reported by this author are based on uptake times of 24 hours or less, and may not represent equilibrium conditions. The highest kinetic BCF value reported by this author, 18,960, may be irrelevant because it was calculated based on a "slow" rate of elimination of residual radioactivity by the fish. According to this study, the fish eliminated 98-99% of the initial load of radioactivity (from the uptake of ^{14}C-labeled TPP) in 9 days. The remaining 1-2% was eliminated more slowly. Because only the total amount of radioactivity was measured without identifying specific radioactive compounds present, it is not certain that the residual radioactivity was due to unchanged TPP and not to metabolites.

Adequate studies are available for goldfish and killifish (Sasaki et al., 1981, 1982). In these two studies, the authors measured BCFs under both static and flow-through conditions, with varying TPP concentrations, and over differing lengths of time. The authors found that the measured BCFs for killifish were largely independent of these parameters.

Reference	Species	BCF	Key Design Parameters				Comments
			Exp. Type	Range (ppb)	Study Length	T (EC)	
Monsanto Chemical Co, 1982c	Rainbow Trout	271			90 days		

Reference	Species	BCF	Key Design Parameters				Comments
			Exp. Type	Range (ppb)	Study Length	T (EC)	
Mayer, 1981	Rainbow Trout	132-364	Flow-through	0.22, 1.4	90 days		Elimination half life 0.54 days
Muir, 1984	Rainbow Trout	573 931 1368	Static	3.1-50.4	1-24 hours		
Muir et al., 1980	Rainbow trout	2,590 (fast) 18,960 (slow)	Static	50	6 hours	10	River water mixed with dechlorinated tap water, pH 8.12-8.36. Fish were exposed to TPP+water for 6 hours then transferred to clean water. BCF expressed as k(uptake)/k(elimination). k(uptake) = 46.36/hour. Elimination rate slows down at about 9 days with 98-99% eliminated. k(fast)=0.0179/hour; k(slow)=0.00245/hour.
Muir, 1984	Fathead minnow	218 561 1,743	Static	0.8-34.9	1-24 hours		
Sasaki et al., 1981	Killifish	250-500	Static	250 initial	2-3 days	25	
Sasaki et al., 1981	Goldfish	110-150	Static	250 initial	2-3 days	25	

Reference	Species	BCF	Key Design Parameters				Comments
			Exp. Type	Range (ppb)	Study Length	T (EC)	
Sasaki et al., 1982	Killifish	189∀90 193∀79 84∀32	Flow-through (all)	30 20 10	35 days 32 days 18 days	25	BCF is independent of concentration, continuous (flow-through) results correlate to static results (Sasaki, 1981). BCF of phosphate esters tested correlate with Log K_{ow}.

Daphnids:

Conclusion:

The currently available data are not adequate to satisfy the daphnid bioconcentration endpoint.

Basis for Conclusion:

No data are available for the daphnid bioconcentration endpoint.

Green Algae:

Conclusion:

The currently available data are not adequate to satisfy the green algae bioconcentration endpoint.

Basis for Conclusion:

No data are available for the green algae bioconcentration endpoint.

Oysters:

Conclusion:

The currently available data are not adequate to satisfy the oysters bioconcentration endpoint.

Basis for Conclusion:

No data are available for the oysters bioconcentration endpoint.

Earthworms:

Conclusion:

The currently available data are not adequate to satisfy the earthworm bioconcentration endpoint.

Basis for Conclusion:

No data are available for the earthworm bioconcentration endpoint.

Fish Metabolism:

Conclusion:

The metabolism rate in fish has not been adequately characterized, and the metabolites have not been adequately identified.

Basis for Conclusion:

None of the studies summarized here identifies any metabolites. All of the studies were designed to monitor the levels of TPP (as either the natural isotope or ^{14}C labeled) in fish to document the rates of uptake and elimination. Although these studies provide information about the rate of elimination of TPP and/or its carbon-containing metabolites from fish, none of these studies adequately describe how TPP is metabolized and what products are formed.

Species	Rate	Comment	References
Rainbow trout	98-99% eliminated in 9 days Rate constant = 0.0179/hour Slower elimination after 9 days Rate constant = 0.00245/hour		Muir et al., 1980
Rainbow trout	Elimination half-life is 0.54 days		Mayer et al, 1981
Killifish	Elimination half-life 1-2 hours		Sasaki et al., 1982

Species	Rate	Comment	References
Killifish	Apparent metabolism is much faster in killifish than in goldfish.	Concentration of TPP in water decreased in the presence of fish. 0% applied TPP remains in the water after ~72 hours. Control (no fish) has no change in TPP concentration.	Sasaki et al., 1981
Goldfish	Apparent metabolism is much slower than in killifish.	60-65% applied TPP remains in the water after 100 hours in presence of goldfish.	Sasaki et al., 1981

Degradation and Transport

Photolysis in the Atmosphere:

Conclusion:

The currently available data are not adequate to satisfy the photolysis in the atmosphere endpoint.

Basis for Conclusion:

No data are available for the photolysis in the atmosphere endpoint

Photolysis in water:

Conclusion:

The available studies do not adequately describe the photolysis behavior of TPP in water under normal environmental conditions. However, this endpoint appears to be adequately characterized.

Basis for Conclusion:

Since triphenyl phosphate does not absorb light at wavelengths above 290 nm, direct photolysis in sunlight is not expected. Three published photolysis studies were located. Similar rate constants and half-lives are reported. For two of these studies, the light from the lamps was not filtered to block wavelengths <290 nm in either experiment (Hg lamps emit at 254 nm), and the results are not environmentally relevant. For the third, the rate constant for photolysis was found to be 34 times greater than phenol with a quantum yield of 0.290 at 254 nm (Wan et al., 1994).

Photolysis of Aqueous Triphenyl Phosphate Irradiated with Low-Pressure Hg Lamps		
Initial concentration: 0.1 ppm pH: 3 and 10	Pseudo 1st-order rate constant was >40/hour ($t_{1/2}$ <1.04 minutes) at both pH levels. Some hydrolysis may occur at pH 10	Ishikawa et al., 1992
Initial concentration: $3.0x10^{-4}$ M pH: 3.4 Time: 6 hours	TPP removed: 100% PO_4^{3-} detected: 60% of theoretical max. Phenol detected: 0%	Ishikawa et al., 1992
Initial concentration: $3.0x10^{-4}$ M pH: 12 Time: 6 hours	TPP removed: 100% PO_4^{3-} detected: 60% of theoretical max. Phenol detected: 9% of theoretical max.	Ishikawa et al., 1992
Initial concentration: 1.0 ppm	Rate constant: $1.9x10^{-2}$/second Half-life: 0.6 minutes	Hicke and Thiemann, 1987

Photolysis in Soil:

Conclusion:

The currently available data are not adequate to satisfy the photolysis in soil endpoint.

Basis for Conclusion:

No data are available for the photolysis in soil endpoint

Aerobic Biodegradation:

Conclusion:

The biodegradation of TPP under aerobic conditions has been adequately characterized.

***Basis for Conclusion*:**

The key study was performed according to OECD guidelines. Additional studies are available, in which TPP is degraded under a variety of conditions. TPP was also found to be ready biodegradable in experimental studies.

Study Type/ Method	Innoculum	Acclim.	Degradation	Time	Comments	Reference
OECD 303A	Activated sludge	14 days	93.8% as DOC removal	20 days	Initial concentration 5 ppm, emulsified with octanol	Ciba-Geigy, Ltd., 1983

Study Type/ Method	Innoculum	Acclim.	Degradation	Time	Comments	Reference
SCAS	Activated sludge		>95%	24 hours		Monsanto Chemical Co., 1980
River die-away			50%	2-4 days		Monsanto Chemical Co., 1980
CO_2 evolution	Activated sludge	14 days	82%	27 days	Initial concentration 22 ppm	Mayer et al., 1981
CO_2 evolution	Activated sludge	14 days	61.9% 81.8%	7 days 28 days	Initial concentration 18.3 ppm	Saeger et al., 1979
Simulated biological treatment/ SCAS	Activated sludge w/ domestic sewage feed		95%	24 hours		Mayer et al., 1981
Simulated biological treatment/ SCAS	Activated sludge w/ domestic sewage feed		93-96%	24 hours	12-week test duration, acclimation time not reported	Saeger et al., 1979
River die-away	River/lake water	20-day lag time	100% as TPP removal by GC analysis	7-8 days	Seneca River water pH 8.2, Lake Onondaga water pH 7.8, Lake Ontario water pH 8.2, all NY sources; hydrolysis may interfere with measurement at higher pH	Howard and Deo, 1979

Study Type/ Method	Innoculum	Acclim.	Degradation	Time	Comments	Reference
River die-away	Mississippi River water		50% primary biodegradation	2-4 days	Initial concentration 0.05 ppm	Mayer et al, 1981
River die-away	Mississippi River water		100%	1.75 days	Initial concentration 1.0 ppm	Saeger et al., 1979
MITI II	Sewage sludge		83-94%	28 days		Chemicals Inspection & Testing Institute, 1992

Anaerobic Biodegradation:

Conclusion:

The currently available data are not adequate to satisfy the anaerobic biodegradation endpoint.

Basis for Conclusion:

No data are available for the anaerobic biodegradation endpoint.

Porous Pot Test:

Conclusion:

The currently available data are not adequate to satisfy the porous pot test endpoint.

Basis for Conclusion:

No data are available for the porous pot test endpoint

Pyrolysis:

Conclusion:

The pyrolysis products of triphenyl phosphate have not been adequately described.

Basis for Conclusion:

No formal pyrolysis studies have been located in the literature.

Pyrolysis Products	Reference
Products include phosphorous oxide	Lewis, 2000 (Sax's Dangerous Properties of Industrial Materials)

Hydrolysis as a Function of pH:

Conclusion:

The hydrolysis data are adequate.

Basis for Conclusion:

Triphenyl phosphate is rapidly hydrolyzed at high pHs, more slowly hydrolyzed at neutral pH, and only very slowly hydrolyzed at acidic pHs. The rates measured under alkaline conditions (pH ~9) are in good agreement with one another, and the rates measured under acidic conditions (pH ~5 or lower) are in reasonable agreement with one another. The results for hydrolysis at pH 7 have been reported to be 19 days, 1.3 years, and 406 days. There is no apparent reason for this discrepancy in values. It appears that the half-life of 19 days was measured once (Mayer et al., 1981) and has then been repeated in other sources. The longer half-life (ca. 1.3 years) has been reported (within acceptable experimental error) in two independent studies (Mabey and Mill, 1978), and is consistent with the observation in Howard and Deo (1979) that the half-life at pH 6.7 was too slow for accurate measurement over the course of the study (14 days).

$T_{1/2}$	pH	Temp.	Comment	Reference
19 days 3 days	7 9	25EC		Mayer et al., 1981
7.5 days 1.3 days	8.2 9.5	21EC	Half-life was too slow for accurate measurement at pH 4.5 and 6.7. Diphenyl phosphate was the only hydrolysis product identified	Howard and Deo, 1979

$T_{1/2}$	pH	Temp.	Comment	Reference
1.3 years	7	25EC	Rate constant = $1.7x10^{-9}$/sec at pH 7	Mabey and Mill, 1978
>28 days 19 days 3 days	5 7 9			Monsanto Chemical Co., 1980
366 days 406 days <5 days	3 7 9	20EC		Ciba-Geigy, Ltd., 1984
630 days 1,125 days <10 days	3 7 9	10EC		Ciba-Geigy, Ltd., 1984
28 days 19 days 3 days	5 7 9	25EC		Mayer et al., 1981, cited in Anderson et al., 1993

Sediment/Water Biodegradation:

Conclusion:

The biodegradation of triphenyl phosphate in the presence of pond and/or river sediment under various conditions has been adequately characterized.

Basis for Conclusion:

Biodegradation of TPP has been studied under a variety of conditions and temperatures in the presence of both river and pond sediment.

Sediment	Temp.	$T_{1/2}$	Comments	Reference
Pond soil	25	50-60 days	Aerobic conditions. Sediment is described to be hydrosoil from a small pond. Initial concentration, 0.05 ppm Major product is diphenyl phosphate.	Muir et al., 1989

Sediment	Temp.	$T_{1/2}$	Comments	Reference
Pond sediment	25 10 2	2.8 days 2.8 days 11.9 days	Static conditions (air/oxygen neither excluded nor added during the test). Sediment was collected from a eutrophic farm pond near Winnipeg, Manitoba. Initial TPP concentration 0.10 :g/mL. Sediment:water ratio 1:10.	Muir et al., 1989
River sediment	25	7.0 days	Static conditions (air/oxygen neither excluded nor added during the test). Sediment was collected from the Red River near Winnipeg, Manitoba. Initial TPP concentration 0.10 :g/mL. Sediment:water ratio 1:10.	Muir et al., 1989
Pond sediment	25	56.7%, 3 days* 13.1%, 40 days*	Aerobic conditions (respirometer, aerated). Initial TPP concentration 0.05 :g/mL Sediment:water ratio 1:20 *Half-life not reported. Values are % TPP remaining over time.	Muir et al., 1989
River sediment	25	68.9%, 3 days* 10.3%, 40 days*	Anaerobic conditions (respirometer, under N_2). Initial TPP concentration 0.05 :g/mL Sediment:water ratio 1:20 *Half-life not reported. Values are % TPP remaining over time.	Muir et al., 1989

Soil Biodegradation with Product Identification:

Conclusion:

The biodegradation rate of triphenyl phosphate in soil has been adequately characterized.

Basis for Conclusion:

The biodegradation of TPP has been studied under aerobic and anaerobic conditions. The biodegradation products have been adequately characterized.

Biodegradation of Triphenyl Phosphate in a Loamy Sand Soil at 20EC					
	Percent TPP Remaining Over Time, HPLC				
Conditions	13 Days	32 Days	60 Days	101 Days	Metabolites Identified
Aerobic	69.3	46.6	30.4	20.2	Diphenyl phosphate, CO_2
Anaerobic		50.2	35.4	31.4	Diphenyl phosphate, CO_2, phenol
Reference: Anderson et al., 1993					

Indirect Photolysis in Water:

Conclusion:

The currently available data are not adequate to satisfy the indirect photolysis in water endpoint.

Basis for Conclusion:

No data are available for the indirect photolysis in water endpoint

Sediment/Soil Adsorption/Desorption:

Conclusion:

The K_{oc} has been adequately characterized.

Basis for Conclusion:

The K_{oc} has been studied in a variety of soil types.

K_{oc}	**Soil Type**	**Reference**
2514	silty clay	Anderson et al., 1993 All measurements were made at 20EC.
3561	loamy sand	
2756	silt loam	

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